

REARRANGEMENTS OF SOME BICYCLIC SYSTEMS

being a thesis presented to the University of
Glasgow for the Degree of Doctor of Philosophy

by

John C. Fairlie

under the supervision of Dr. R. McCrindle.

ProQuest Number: 11011860

All rights reserved

INFORMATION TO ALL USERS

The quality of this reproduction is dependent upon the quality of the copy submitted.

In the unlikely event that the author did not send a complete manuscript and there are missing pages, these will be noted. Also, if material had to be removed, a note will indicate the deletion.



ProQuest 11011860

Published by ProQuest LLC (2018). Copyright of the Dissertation is held by the Author.

All rights reserved.

This work is protected against unauthorized copying under Title 17, United States Code
Microform Edition © ProQuest LLC.

ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 – 1346

Summary

This thesis deals with some aspects of the rearrangements of bridged bicyclic systems.

The acetolysis of erythroxylool B toluene-p-sulphonate (31, R=OTs) has been studied (Chapter 1.). The 1-bicyclo (3,2,1) octylcarbinyol system rearranges with ring expansion to the substituted bicyclo (3,3,1)- and bicyclo (3,2,2) nonyl derivatives (38 and 33, R=OAc). Dihydroerythroxylool B tosylate (44, R=OTs) rearranges in an analogous manner. It is proposed that these reactions may involve bridged carbonium ions.

In an attempt to interconvert the known tetracyclic diterpenes, kaurene (51) has been treated with formic acid (Chapter 2.). The three products isolated are all stachane formates (56, 58 and 60, R=OF) the substituent being located at C-15, C-16 or C-12 in the stachane skeleton. The 12-formate arises from a net 1,3-hydride shift from C-12 to C-16.

The buffered acetolysis of exo-bicyclo (3,2,1) octane-6-toluene-p-sulphonate (93, R=OTs) has been found to give exo-2-bicyclo (3,2,1) octyl acetate, 40% (100, R=OAc) 2-bicyclo (2,2,2) octyl acetate, 44% (101, R=OAc) and exo-6-bicyclo (3,2,1) octyl acetate, 16% (93, R=OAc),

whereas the corresponding endo-6-isomer gave (100, R=OAc) 19% (101, R=OAc), 21% and (93, R=OAc) 60% (Chapter 3.). The significance of these results is discussed in terms of a 4,6-hydride shift in the bicyclo (3,2,1) octane skeleton. Bridged cations (or equivalents) are postulated to be involved in these reactions. The rates of solvolysis of these toluene-p-sulphonates have been determined.

A possible π -route to the 6-bicyclo (3,2,1) octyl cation has been examined by solvolysis of 3- Δ^3 cyclopentenyl propyl toluene-p-sulphonate (131, X=OTs) in acetic acid (Chapter 4.). Using either sodium acetate or urea as a buffer no bicyclic acetates were detected from the reaction the sole product being the corresponding primary acetate.

The reduction of syn-bicyclo (2,2,2) oct-5-en-2-yl toluene-p-sulphonate (143, X=OTs) with lithium aluminium hydride in refluxing diethyl ether has been found to give bicyclo (3,2,1) oct-2-ene (146) (Chapter 5.). The corresponding anti-toluene-p-sulphonate (144, X=OTs) under identical conditions also gave a major product with a modified skeleton, namely tricyclo (3,2,1,0^{2,7})-octane (147). Further examination of the reaction using deuterium labelled compounds led to the conclusion that long-lived ionic intermediates are not involved.

Acknowledgements

I should like to thank my supervisor Dr. R. McCrindle for his guidance and encouragement during the course of this work. I am also indebted to Dr. R. A. Appleton for his support and to Drs. K. H. Overton and W. Parker for useful discussions. Thanks are also due to Miss H. R. Derry who typed this thesis.

Contents

CHAPTER 1. The rearrangement of neopentyl systems.

Introduction	1.
Acetolysis of erythroxylo1 B tosylate						12.
Experimental	24.
Diagrams	39.

CHAPTER 2. The rearrangement of tetracyclic diterpenes.

Introduction and Discussion				40.
Experimental	52.
Diagrams	55.

CHAPTER 3. Hydride shifts in bicyclic systems.

Introduction	56.
Solvolysis of <u>exo</u> and <u>endo</u> 6-bicyclo (3,2,1) octyl tosylates	67.
Rate Studies	84.
Experimental	91.
Diagrams	102.

CHAPTER 4. Π -routes to bicyclic systems.

Introduction	103.
π -route of the 6-bicyclo (3,2,1) octyl								
cation	109.
Experimental	113.
Diagrams	119.

CHAPTER 5. Rearrangements during reduction of
toluene-p-sulphonates.

Introduction	120.
Reduction of bicyclo (2,2,2) oct-5-en-2-yl tosylates	129.
Experimental	137.
Diagrams	142a.
References	143.

NEOPENTYL SYSTEMS

When a primary sulphonate or halide function is adjacent to a fully substituted carbon atom there is a considerable tendency for ionisation of the molecule to lead to tertiary substituted products via rearrangement of the intermediate carbonium ion species. The simplest examples of this system are neopentyl derivatives (1) which react¹ under conditions involving carbonium ion intermediates to give products derived from the t-amyl cation (3).

Various neopentyl systems have been studied for example in the acyclic (4)², the monocyclic (5)³ (6)⁴ and (7)⁵ and the bicyclic (8)⁶, (9)⁷ and (10)⁷ series.

Recently two groups of workers^{8,9} have established by isotopic labeling that the parent neopentyl system rearranges without complication by such possibilities as 1:3-hydride shifts. Thus the neopentyl rearrangement

proceeds entirely by a 1,2-methyl shift. There has been some controversy over whether the neopentyl cation (2) exists as an intermediate in the reaction or whether a concerted mechanism involving methyl participation (transition state 2a) operates¹⁰.

It is known that ethyl tosylate solvolyses without rearrangement even in a weakly nucleophilic solvent such as formic acid¹¹, there being no hydrogen participation. Ethyl tosylate reacts faster than neopentyl tosylate in more nucleophilic solvents, but in formic acid, however, the rates are almost identical. Winstein¹⁰ suggested that even in formic acid the ionisation of ethyl tosylate will be assisted by nucleophilic solvent participation, which is sterically denied to neopentyl tosylate. Thus some other rate-enhancing factor must be influencing ionisation of the latter. He argued against inductive

and steric effects and concluded that methyl participation is involved. This view has been endorsed by other workers^{2,12}. The acetolysis rates for a series of 2,2 dimethylalkyl brosylates² (4) increase as the bulk of R is increased and this was attributed to carbon participation with a resultant relief of strain in the intermediate.

There is some stereochemical evidence to support the intervention of a concerted mechanism in the rearrangement of neopentyl derivatives. Thus, optically active neopentanol-1-d¹³ undergoes dehydration to give optically active 2-methyl-1-butene -3-d along with other products and under solvolytic conditions resolved neopentyl-1-d tosylate¹⁴ rearranges to optically active products. Although these results would suggest that a bridged-ion, or equivalent, is involved in the rearrangement it is possible that the

primary carbonium ion formed by simple ionisation, rearranges so fast as to preclude any rotation about the adjacent C-C bond which would lead to racemic products¹⁴.

The fact that little, if any, unrearranged products are isolated from carbonium ion reactions of neopentyl systems is a necessary but not a sufficient criterion for participation and it may well be that the speed of rearrangement of a primary carbonium ion intermediate eliminates the possibility of solvent capture of that ion.

One piece of evidence against participation centres on the fact that tertiary carbonium ions are much more stable than primary¹⁵, thus the neopentyl rearrangement (1) \longrightarrow (3) should have a considerable driving force. However, the rates of reaction of neopentyl derivatives are approximately the same as those of the corresponding ethyl derivatives and so,

at best, the rate-enhancing factor is small. There is some evidence¹⁵ that, contrary to Winstein (*vide supra*), the rate enhancement is inductive in origin. Thus the small rate differences recorded cannot be considered strong evidence for a mechanism involving participation.

Schleyer¹⁶ has examined the feasibility of participation being involved in these reactions, by a study of the solvolysis of 1-adamantylcarbinyl tosylate (11, X=OTS). Unlike most molecules this should have a considerable reluctance to rearrange as this would lead to the tertiary homoadamantyl cation (12) with loss of the exceptional strain-free properties of the adamantane skeleton¹⁷. In other words the transformation (11) \longrightarrow (12) should be much less favourable than the analagous rearrangement (1) \longrightarrow (3) in the parent neopentyl system. Schleyer argued that the solvolyses of neopentyl tosylate (1, X=OTS) and 1-adamantyl tosylate (11, X=OTS)

should have the same rates if the rate-determining steps involve simple ionisation, but that the neopentyl system should solvolyse faster if the initial intermediate is the result of ionisation with participation of an adjacent group. The products isolated from the acetolysis of 1-adamantyl-carbonyl tosylate¹⁶ (11, X=OTS) were the unrearranged acetate (11, X=OAC) and the tertiary acetate (13) in the respective percentages of 7 and 93. Further, the proportions of products do not alter with varying nucleophilicity of solvent and this suggests that the primary product (11, X=OAC) is derived from the corresponding carbonium ion. Schleyer concluded from this that the reaction proceeds by simple ionisation of (11, X=OTS), then partial or complete equilibration of the primary ion with the homoadamantylcation (12) followed by solvent capture to give the isolated products. As would be expected

from this mechanism the rate of acetolysis of 1-adamantylcarbonyl tosylate was found to be similar to that of its neopentyl equivalent, and indeed is slightly faster, presumably because of inductive effects. Thus it seems likely that neopentyl derivatives have little tendency to rearrange via a bridged ionic intermediate.

Winstein³ recognised that participation in neopentyl systems might be enhanced if relief from steric strain is thereby obtained. In particular the rates of solvolysis of the compounds (5, X=OTs)³ (9, X=OTs)⁷, and (10, X=OTs)⁷ are respectively 3×10^7 , 180 and 1500 times faster than that of neopentyl tosylate. Although these enhancements are relatively small in comparison to the total driving force derived from relief of angle strain by ring expansion Schleyer¹⁶ concedes that in these types of constrained neopentyl systems the enhanced rates may be due to a change in mechanism from unassisted to assisted ionisation.

Of particular interest in view of the work reported below are the rearrangements of 1-carbinyl tosylate bridged bicyclic compounds, of which (14)¹⁸, (15)^{18,19}, (16)²⁰, (17)^{20,21}, (18)^{20,21}, (19)²² have been studied. Most of these compounds undergo ring expansion under solvolytic conditions to the bridgehead substituted product. Accordingly, (14) solvolyses in acetic acid to 1-bicyclo (2,2,1) heptyl acetate (20), (15) to 1-bicyclo (2,2,2) octyl acetate (21) and (16) to 1-bicyclo (3,2,2) nonyl acetate (22). The heterocyclic compound (17) reacts via ring expansion followed by fragmentation, whereas the corresponding quaternary salt₍₁₈₎ solvolyses slowly without rearrangement as a consequence of the positively charged nitrogen atom.

The bicyclo (3,3,1) nonyl system is relatively stable and therefore ring expansion during the acetolysis of (19, X=OTS) will not be so favoured as in

the other bridged bicyclic compounds discussed. This is evident in the large percentage (36%) of unrearranged product (19, X=OAC) formed in the reaction together with the ring-expanded products (23) (22%) and (24) (37%)²². Another product isolated in minor amount (5%) from this reaction is the secondary acetate (25). This represents a further mode of reaction of these systems, the net result being a 1:3 hydride shift from C-9 to the carbonyl group (a type of process not found in the case of neopentyl tosylate^{8,9}). The compound (26) arising from the equivalent of a 1:3 hydride shift from C-2 is produced in only trace amounts.

In the rearrangements of these bridged bicyclic carbonyl derivatives factors are involved which are not present in the simple acyclic and monocyclic neopentyl systems. Any mechanism involving formation of a discrete primary cation followed by rapid alkyl shift

seems unlikely as this would involve a bridgehead carbonium ion as an intermediate, thus contravening Bredt's²³ rules. Although bicyclo (3,3,1) non-1-ene (27) has been prepared²⁴ there is little evidence to support the existence of trigonal bridgehead carbon atoms in smaller bicyclic ring systems, for example, the decarboxylation of (28) and (29) is thought to involve a non-enolic intermediate²⁵. Also it becomes evident from an examination of models that these ring expansion reactions involve the inversion of the bridgehead carbon atom, a process which would appear unfavourable via a classical Wagner-Meerwein shift.

It seems likely that in the rearrangement of these bridgehead carbonyl tosylates, especially the smaller ring compounds (14) and (15), the intermediate is a bridged ion. Ionisation of (15) accompanied by participation of the C-1-C-7 bond would lead to (30) which without undergoing further rearrangement could

suffer solvent capture at C-1 to give the product (21) and as C-1 is trigonal in the bridged intermediate (30) the facile inversion of this carbon atom is explained. The fact that compounds (14) and (15) appear to solvolyse with rate enhancement may support the intervention of a bridged intermediate. However, it is possible that this enhancement may be a result of freer access of solvent to the ionisation sites than in the parent neopentyl system.

Acetolysis of erythroxylo1 B tosylate.

Erythroxylo1 B (31) was isolated from the tree ethroxyl monogynum by McCrindle and Murray^{26,27}. It is a tetracyclic diterpenoid alcohol with the constitution shown, the C and D rings basically forming a 1-bicyclo (3,2,1) octylcarbiny1 system. Thus this compound appeared potentially useful for a study of the solvolysis of these bridgehead hydroxy methyl derivatives as it seemed unlikely that the A and B rings would participate to a marked extent in such reactions.

Accordingly erythroxylo1 B (31, R=OH) was separated from its congener erythroxylo1 A (32) by gradient elution chromatography and converted to the corresponding tosylate (31, R=OTS) by reaction with toluene-p-sulphony1 chloride in pyridine. The tosylate was reacted with buffered refluxing acetic acid for 96 hours and the resulting

acetate products (no hydrocarbons were detected from the reaction) reduced to the corresponding alcohols by treatment with lithium aluminium hydride. The alcohols were separated into two pure components by preparative thin layer chromatography (t.l.c.) using plates $\frac{1}{2}$ metre in length.

The less polar alcohol (33, R=OH) (55% of total alcohol product) showed in its n.m.r. spectrum an AB quartet at τ 4.30 with a coupling constant of $J=9$ c./sec. suggestive of a disubstituted olefin in a six-membered ring²⁸. The three methyl groups appeared as singlets above τ 9. The absence of carbinol protons in the n.m.r. spectrum and an absorption at 3615 cm^{-1} in the i.r.²⁹ confirmed the presence of a tertiary hydroxyl function.

This alcohol was converted by treatment with acetic anhydride in refluxing acetic acid into an acetate (33, R=OAc) which was stable to the acetolysis conditions, and shown by a combination of gas chromatography and mass spectrometry

(g.c. m.s.) to be identical to the more abundant product formed from the acetolysis of erythroxylo1 B. This acetate (33, R=OAC) exhibited a quartet at τ 4.24 in its n.m.r. spectrum, corresponding to the olefinic protons and a three proton singlet at τ 8.06 for the acetate methyl.

Hydrogenation of the alcohol over Pd/C catalyst resulted in the uptake of one molar equivalent of hydrogen and the formation of the dihydro alcohol (34, R=OH).

Treatment of the parent alcohol (33, R=OH) with diborane³⁰ and oxidation of the resultant boron complexes with peroxide yielded a mixture of two diols (35 and 36). The n.m.r. spectrum of the β -diol (35) featured a broadened doublet at τ 5.88 assigned to the carbinol proton at C-15, however the conformation mobility of the system precludes any exact prediction of the relevant dihedral angles between the carbinol proton and neighbouring methylene protons.

The absorptions at 3639 cm^{-1} and 3614 cm^{-1} in the i.r. indicated the presence of two free hydroxyl functions. The α -diol (36) showed absorption at 3612 cm^{-1} and 3540 cm^{-1} the lower value resulting from hydrogen bonding of the hydrogen of the secondary to the oxygen of the tertiary hydroxyl group³¹. The stereochemistry shown for the secondary functions is predicted from a consideration of the steric course of the hydroboration reaction³⁰.

Oxidation of the β -diol (35) with Jones reagent³² afforded the ketol (37). An absorption at 1714 cm^{-1} in the i.r. indicative of a cyclohexanone confirmed that the double bond of the rearrangement product (33) is in a six-membered ring.

The more polar alcohol (38, $R=OH$) (45% of total alcohol product) from the reduction of the acetolysis products has three methyl groups which resonate above $\tau 9$ in its n.m.r. spectrum. A sharp singlet at $\tau 4.47$

and a broad singlet at τ 7.85 each integrating for two protons correspond respectively to the olefinic protons at C-15 and C-16 and the allylic methylene group at C-17. The absence of significant spin-spin coupling between the allylic and olefinic protons is somewhat surprising. The broadening of the allylic methylene singlet is probably the result of long-range coupling to protons on C-14 and C-12 as an examination of models indicates that certain of these protons have the requisite 'W' geometry for such interactions³³.

This more polar alcohol (38, R=OH) was converted into an acetate (38, R=OAC) identical (by g.c. m.s.) to the less abundant (45%) compound formed in the acetolysis of erythroxy1 B tosylate (31, R=OTS). It was stable to the acetolysis conditions. The olefinic protons of this acetate (38, R=OAC) resonate as a two proton singlet at τ 4.46 and the allylic protons as an AB quartet at τ 7.45 with a geminal spin-spin coupling constant of

16c./sec.³⁴.

The alcohol (38, R=OH) took up one molar equivalent of hydrogen over a Pd/C catalyst to give the saturated compound (39, R=OH).

Hydroboration of the unsaturated alcohol (38, R=OH) yielded essentially a single product (40, R=OH) the i.r. spectrum of which indicated the presence of two free hydroxyl functions absorbing at 3613 cm^{-1} and 3635 cm^{-1} . This diol was converted to the hydroxyacetate (40, R=OAC) by treatment with acetic anhydride in pyridine at room temperature for three hours. The proton at C-16 in (40, R=OAC) resonates at $\tau 4.67$ and has a coupling pattern similar to the endo 3-proton in 3-substituted bicyclic nonanes³⁵.

Oxidation of the diol (40, R=OH) furnished the ketol (41) which as expected exhibited a carbonyl absorption frequency in the i.r. indicative of a cyclohexane at 1715 cm^{-1} .

The alcohol (38, R=OH) was treated with selenium dioxide in refluxing aqueous dioxan³⁶ to confirm the presence of the methylene group, as this could not be achieved by n.m.r. due to the absence of spin-spin coupling of that group to the olefinic protons. The product (42) from this reaction shows absorption in the i.r. at 3600 and 3535 cm^{-1} confirming the vicinal nature of the hydroxy functions. The C-17 carbinol proton exhibited no coupling to the olefinic protons but is broadened by long-range coupling to a proton at C-14. This unsaturated diol (42) was oxidised by manganese dioxide to the hydroxy enone (43) the olefinic protons of which are magnetically non-equivalent, the proton at C-16 resonating at τ 3.85, $J = 10$ c./sec. and that at C-15 at τ 2.98. Carbonyl absorption in the i.r. at 1685 cm^{-1} and u.v. activity at 238 $\text{m}\mu$ ($\log \epsilon = 3.8$) characteristic of an enone confirms the structure of (43).

Erythroxylo1 B was hydrogenated to the saturated compound (44, R=OH), and the derived tosylate heated with buffered acetic acid. The two acetate products from this reaction were shown (g.c. m.s.) to be identical in constitution and proportion to the mixture of acetates (i.e. 34 and 39) obtained by hydrogenating the products from the acetolysis of erythroxylo1 B tosylate (31, R=OTs). In other words, the acetolysis of erythroxylo1 B tosylate (31, R=OTs) and dihydroerythroxylo1 B tosylate (44, R=OTs) are completely analagous, the double bond in the case of the former apparently having little or no effect on the product distribution.

The rates of acetolysis of these two tosylates (31 and 44), (R=OTs) at 100°C were determined by the spectrometric method of Swain and Morgan³⁷ described in greater detail in section 3. The dihydro compound (44, R=OTs) exhibited good first-order rate behaviour and had a rate constant of $k^{100} = 21.23 \pm 0.60 \times 10^{-6} \text{ sec.}^{-1}$

which is about twelve times faster than the parent neopentyl tosylate (1, X=OTS)¹⁶ at the same temperature. Although good first-order behaviour was not obtained for the acetolysis of erythroxylo1 B tosylate (31, R=OTS) an approximate rate constant of this tosylate $k^{100} = 4 \times 10^{-7}$ sec.⁻¹ allowed an estimation of the relative reactivities of the two tosylates, the unsaturated compound being some 50 times less labile than derived saturated tosylate.

There appeared to be three possible courses of reaction during solvolysis of erythroxylo1 B tosylate; (31, R=OTS) and its dihydro analogue; (a) bimolecular displacement of the tosylate function by solvent or acetate ion to give the unrearranged product (31, R=AC)^{16,22}; (b) ring expansion to give tertiary bridgehead acetates^{18,19,20} or; (c) hydride shift to give secondary substituted products with the formation of an additional methyl group in the molecule²².

From an examination of the products it is evident that only process (b) occurs.

In the formation of both products the angle strain associated with a five-membered ring has been relieved thus suggesting that this may accelerate the reaction³. In this context it is noteworthy that the solvolysis of dihydro-erythroxy B tosylate (44, R=OTS) is faster than that of the corresponding neopentyl compound. Although the presence of the A and B rings in the former may influence the rate it appears from an examination of models that this is unlikely. The slower rate of acetolysis of erythroxy B tosylate (31, R=OTS) is much as would be expected³⁸ if the double bond takes no part in the intermediates and exhibits only the normal inductive retarding effect. This evidence points to the possibility of bridged ions as the product-forming intermediates in these reactions.

This is substantiated by the structure of the products. It seems unlikely that (34, R=OAC) and (39, R=OAC) would be formed during the acetolysis of (44, R=OTS) by simple ionisation of the tosylate followed by discrete alkyl shifts as this mechanism would necessitate the intermediacy of bridgehead carbonium ions, and does not account for the relatively facile inversion of the bridgehead carbon atom. Rather it appears more feasible for the tosylate function in (44, R=OTS) to ionise with participation of either the C-13 - C-16 bond to form intermediate (45) or the C-13 - C-14 bond to form a separate bridged cation (46) the relief of steric strain in the five-membered ring being the driving force for the involvement of these two bonds to the exclusion of the C-12 - C-13 bond. Ions (45) and (46) will then undergo acetate capture at C-13 to furnish the isolated products (39) and (34) respectively.

Acetate capture of C-17 which would lead to unrearranged product, will not occur as this position is blocked by the departing tosylate group.

The intermediate in the rearrangement of erythroxylo B tosylate (31, R=OTS) to (33, R=OAC) will be similar, but the formation of (38, R=OAC) is more complicated in that a vinylagous group is migrating and in particular an sp^2 hybridised bond is assisting ionisation of the tosylate. Nevertheless, a bridged intermediate can be postulated in this case and an orbital representation of such an ion is shown (47). In this, the vacant sp^2 orbital at C-16 overlaps with the two p-orbitals at C-13 and C-17 (much in the same way as an sp^3 orbital is thought to overlap with p-orbitals in a normal bridged ion)³⁹. The filled p-orbitals of the double bond (C-15 and C-16) are then orthogonal to the p-orbitals of the bridged ion (C-13 and C-17) thus precluding any overlap and hence participation of the double bond during acetolysis. This is borne out by the relatively slow rate of solvolysis of erythroxylo B tosylate (31, X=OTS).

Experimental

General:-

Melting points were determined on a Kofler block or where indicated in sealed tubes in a Gallenkamp melting point apparatus.

'Woelm' alumina (neutral) deactivated in the prescribed manner to grade III was used for chromatography. Light petroleum refers to the fraction of b.p. 40-60° and petroleum to the fraction of b.p. 60-80°. Thin-layer chromatoplates were spread with Merck's 'Kiesel gel G', run in 20% ethyl acetate - light petroleum or 5% methanol-chloroform, and developed with a ceric ammonium sulphate spray.

Analytical Gas-liquid Chromatograms of the diterpenoid compounds were obtained on a Pye-Argon chromatograph using 1% S.E.30 and 2% 20M P.E.G. columns. The bicyclic mixtures were analysed on a Perkin-Elmer F-11 instrument

fitted with a carbowax 1540 support-coated open tubular column (50ft.): carrier gas (N_2) flow rate was 4ml./min., and oven temperatures were 50° (hydrocarbons) and 100° (alcohols and acetates).

Combined G.L.C.-mass spectra (G.C.M.S.) analyses were obtained on an LKB 9000 spectrometer. Nuclear magnetic resonance spectra were recorded at a frequency of 60 Mc./sec. on a Perkin-Elmer R.10 and at a frequency of 100 Mc./sec. on a Varian HA-100 spectrometer using dilute solutions (approximately 3 mol. %) in deuteriochloroform, with tetramethyl silane as an internal reference. The calibration of the latter spectrometer was checked using a Hewlett-Packard electronic counter (5212A). Chemical shift values for the methyl resonance (\underline{CH}_3 -CO) of the acetate standards in Chapter 3 were derived from at least five recordings on an expanded scale (2c./sec./cm.) and should be accurate to ± 0.003 p.p.m. The composition of the acetate mixtures was evaluated from peak areas and peak heights in the 8τ region on the above scale expansion (mean of increasing and decreasing field sweep).

The infra-red solution spectra were run in carbon tetrachloride by Mrs. F. Lawrie on a Unicam SP.100 Mark II, or a Perkin-Elmer 225 grating spectrophotometer, routine solution spectra were recorded on a Perkin-Elmer 257 grating spectrophotometer. U.V. spectra were run in ethanol on a Unicam SP.800A instrument.

Microanalyses were by Mr. J. M. L. Cameron, Glasgow, and his staff.

Separation of Erythroxylois A and B (31 and 32, R=OH). -

A mixture of the erythroxylois (25g.) was chromatographed over neutral alumina (III; 1 Kg.) eluting with a solvent of gradually increasing polarity obtained by slow addition of ethyl acetate in light petroleum (1:5) to ethyl acetate in light petroleum (1:20) from this partial separation erythroxylois B (31, R=OH)(3.2g.) m.p. 121-123° (lit.²⁷ m.p. 122-123°), was obtained.

Erythroxylois B acetate. - Erythroxylois B (31, R=OH)

(55mg.) was dissolved in pyridine (3ml.) and acetic anhydride (3ml.) added. After 2 hrs. the reaction mixture was poured onto ice and extracted with ether. The ether extracts were washed with dilute hydrochloric acid and then saturated sodium bicarbonate, dried and the solvent was removed under vacuum. Sublimation of the crude product furnished erythroxylois B acetate (31, R=OAc) (57mg.), m.p. 54-56° (lit.²⁷ m.p. 56-57°).

Erythroxylo1 B tosylate (31, R=OTS).- Chilled solutions of erythroxylo1 B (2.051g.) in dry pyridine (15ml.) and toluene-p-sulphony1 chloride (3g.) in the same solvent (10ml.) were combined and allowed to stand for 16 hrs. The reaction mixture was poured onto crushed ice and the precipitated products filtered off and washed with water. The crude product was recrystallised from methanol to give erythroxylo1 B tosylate (31, R=OTS) (2.2g.) m.p. 128-129° (lit.²⁷ m.p. 128-129°): n.m.r., τ at τ 4.35 (2H-15,16; J=6c./sec.); $\underline{\text{S}}$ at τ 6.13 (2H-17); τ at τ 2.40 (4H-aromatic H's); $\underline{\text{S}}$ at τ 7.57 (3H-aromatic methyl).

Acetolysis of Erythroxylo1 B tosylate.- Erythroxylo1 B tosylate (1.041g.) was treated with refluxing acetic acid (40ml.) containing sodium acetate (1.460g.) for 96 hrs. The reaction mixture was cooled, added to water and extracted with ether. The combined ether extracts were washed with saturated sodium bicarbonate, dried, and the ether was removed. Analysis of the

residue (799 mg.) by g.l.c. (1% S.F.30 at 175°C) showed that this was a mixture (55:45) of two acetates neither of which was erythroxylool B acetate (31, R=Ac). No hydrocarbons could be detected in the reaction mixture.

Reduction of the solvolysis products.- The solvolysis products (780 mg.) were treated with excess lithium aluminium hydride in refluxing diethyl ether for 2 hrs. A saturated aqueous solution of sodium sulphate was then added followed by anhydrous sodium sulphate. Removal of the drying agent and solvent afforded a mixture (681 mg.) of alcohols which were separated on t.l.c. plates 0.5 metres in length.

The less polar component (33, R=OH) (55% of total product) had m.p. 149-151°: n.m.r., τ at 4.30 (2H-15,16; $J = 9\text{c./sec.}$); $\underline{\text{S}}$ at τ 9.15 (6H - two methyls); $\underline{\text{S}}$ at τ 9.18 (3H - methyl): i.r., ν_{max} 3615, 3030 cm^{-1} . (Found: C, 83.2; H, 11.3. $\text{C}_{20}\text{H}_{32}\text{O}$ requires C, 83.3; H, 11.2%).

The more polar alcohol (38, R=OH), m.p. 128-130°: n.m.r., \underline{S} at τ 4.47 (2H-15,16; $W^{1/2} = 2\text{c./sec.}$); \underline{S} at τ 7.85 (2H-17; $W^{1/2} = 3\text{c./sec.}$); \underline{S} at τ 9.13, 9.18, 9.29 (all 3H-methyls): i.r., ν_{max} 3613, 3035 cm^{-1} . (Found: C, 83.2; H, 11.3. $\text{C}_{20}\text{H}_{32}\text{O}$ requires C, 83.3; H, 11.2%).

Acetylation of the less polar alcohol.- The alcohol (33, R=OH) (30 mg.) and acetic anhydride (3 ml.) were reacted in acetic acid (10 ml.) under reflux for 2 hr. The reaction was diluted with water and extracted with chloroform. After removal of the solvent crystallisation of the crude product from methanol yielded the acetate (33, R=OAc) (31 mg.), m.p. 113-116°: n.m.r., \underline{Q} at τ 4.24 (2H-15,16; $J = 10\text{c./sec.}$); \underline{S} at τ 8.06 (3H-acetate methyl): i.r., ν_{max} 1725, 1245 cm^{-1} . (Found: C, 79.7; H, 10.6. $\text{C}_{22}\text{H}_{34}\text{O}_2$ requires C, 79.9; H, 10.4%). This acetate was identical (g.c.m.s.) to the more abundant acetate formed during the acetolysis of erythroxylool B tosylate.

The more polar alcohol (38, R=OH) (32 mg.) was converted by the same method to the acetate (38, R=OAc) (34 mg.), m.p. 105-107°: n.m.r., $\underline{\text{S}}$ at τ 4.46 (2H-15,16); $\underline{\text{Q}}$ at τ 7.45 (2H-17, J = 18c./sec.); $\underline{\text{S}}$ at τ 8.08 (3H-acetate methyl): i.r., ν_{max} . 1725, 1245 cm^{-1} . (Found: C, 79.6; H, 10.4. $\text{C}_{22}\text{H}_{34}\text{O}_2$ requires C, 79.9; H, 10.4%). This acetate is the less abundant acetate (g.c.m.s.) produced by the action of buffered acetic acid on erythroxylool B tosylate (31, R=OTS).

Hydrogenation of the less polar alcohol (33, R=OH).- The alcohol (33, R=OH) (29 mg.) was hydrogenated over Pd/C in ethyl acetate with the uptake of one molar equivalent of hydrogen. Removal of the catalyst and solvent afforded the saturated alcohol (34, R=OH) (29 mg.) which was purified by crystallisation from light petroleum m.p. 142-143.5° (sealed tube): n.m.r., $\underline{\text{S}}$ at τ 9.03 (3H-methyl); $\underline{\text{S}}$ τ 9.14 (6H-two methyls): i.r., ν_{max} . 3612 cm^{-1} . (Found: C, 82.4; H, 11.9. $\text{C}_{20}\text{H}_{34}\text{O}$ requires C, 82.7; H, 11.8%).

Hydrogenation of the more polar alcohol (38, R=OH).-

The alcohol (38, R=OH) (32 mg.) was hydrogenated as above with the uptake of one molar equivalent of hydrogen. Crystallisation of the product from light petroleum furnished the saturated alcohol (39, R=OH), m.p. 136-140°: n.m.r., $\underline{\text{S}}$ at τ 9.08 (3H-methyl); $\underline{\text{S}}$ at τ 9.18 (6H-two methyls): i.r., ν_{max} 3613 cm^{-1} . (Found: C, 83.0; H, 11.9. $\text{C}_{20}\text{H}_{34}\text{O}$ requires C, 82.7; H, 11.8%).

Hydroboration of the less polar alcohol.- The alcohol (33, R=OH) (200 mg.) was dissolved in dry diethyl ether (20 ml.) containing boron trifluoride etherate (3 ml.). Lithium aluminium hydride (300 mg.) in diethyl ether was then added dropwise to the stirred solution over a period of 15 min., the reaction being maintained under an atmosphere of nitrogen. After 14 hr. saturated sodium sulphate was added to the solution, then anhydrous sodium sulphate. Filtration and removal of the ether furnished the boron complexes. These were dissolved in

10% methanolic sodium hydroxide (20 ml.), 30% hydrogen peroxide (2 ml.) was added dropwise and the reaction stirred for 90 min. The volume was reduced by removal of solvent under vacuum, water was then added and the product extracted into ether. Evaporation of the ether afforded a mixture of diols (184 mg.) (35 and 36), which were separated by t.l.c.

The α -diol (36).- purified by sublimation had m.p. 157-160°; n.m.r., M at τ 6.16 (1H-16); S at τ 9.08, 9.17 and 9.17 (all 3H-methyls): i.r., V_{\max} . 3612 and 3540 cm^{-1} . (Found: C, 78.0; H, 11.1, $\text{C}_{20}\text{H}_{34}\text{O}_2$ requires C, 78.4; H, 11.2%).

The β -diol (35).- crystallised from ethyl acetate had m.p. 177-180°: n.m.r., b.d. at 5.88 (1H-16; $J = 7\text{c./sec.}$); S at τ 9.12, 9.16 and 9.21 (all 3H-methyls): i.r., V_{\max} . 3639, 3614 cm^{-1} . (Found: C, 79.1; H, 11.2. $\text{C}_{20}\text{H}_{34}\text{O}_2$ requires C, 78.4; H, 11.2%).

Oxidation of the β -diol (35).— Jones reagent was added dropwise to a chilled solution of the diol (35) (37 mg.) in acetone (5 ml.) until a permanent brown colour indicated that the reaction was complete. The mixture was poured into water and extracted with ether. Crystallisation of the crude product from light petroleum furnished the ketol (37) (30 mg.), m.p. 153-156°: n.m.r., δ at τ 9.12, 9.19 and 9.29 (all 3H-methyls): i.r., ν_{max} . 3608, 1714 cm^{-1} (Found: C, 78.7; H, 10.6. $\text{C}_{20}\text{H}_{32}\text{O}_2$ requires C, 78.9; H, 10.6%).

Hydroboration of the more polar alcohol (38, R=OH).—

The alcohol (38, R=OH) (186 mg.) was treated with diborane and the resulting boron complexes oxidised by the above procedure yielding essentially a single product which was purified by preparative t.l.c. and crystallisation from ethyl acetate to give the diol

(40, R=OH), m.p. 254-256° (decomp.): i.r., ν_{\max} . 3635, 3613 cm^{-1} . (Found: C, 78.3; H, 11.0. $\text{C}_{20}\text{H}_{34}\text{O}_2$ requires C, 78.4; H, 11.2%).

Acetylation of this alcohol (25 mg.) with acetic anhydride in pyridine led to the corresponding monoacetate (40, R=OAc) (23 mg.), m.p. 126-128°: n.m.r., septet at τ 4.67 (1H-16); $\underline{\text{S}}$ at τ 8.04 (3H-acetate methyl): i.r., ν_{\max} . 3614, 1728 cm^{-1} .

Oxidation of the diol (40, R=OH).- The diol (40, R=OH) (43 mg.) was oxidised in chilled acetone by dropwise addition of Jones' reagent. Workup and crystallisation of the crude product from light petroleum furnished the ketol (41) (34 mg.), m.p. 180-182°: n.m.r., $\underline{\text{S}}$ at τ 9.14 (6H-two methyls); $\underline{\text{S}}$ at τ 9.20 (3H-methyl): i.r. ν_{\max} . 3606, 1715 cm^{-1} . (Found: C, 78.5; H, 10.3. $\text{C}_{20}\text{H}_{32}\text{O}_2$ requires C, 78.9; H, 10.6%).

Allylic oxidation of the alcohol (38, R=OH).- The alcohol (38, R=OH) (52 mg.) was treated with selenium dioxide (300 mg.) in refluxing moist dioxan (8 ml.) for 48 hr. The reaction mixture was poured into water and the product extracted into chloroform. The solvent was dried, removed under vacuum and the product crystallised from ethyl acetate to give the unsaturated diol (42) (45 mg.), m.p. 219-220° (sealed tube): n.m.r., S at τ 4.16 (2H-15,16); b.s. at τ 6.38 (1H-17): i.r., ν_{\max} . 3600, 3535, 3020 cm^{-1} . (Found: C, 78.8; H, 10.6. $\text{C}_{20}\text{H}_{32}\text{O}_2$ requires C, 78.9; H, 10.6%).

Oxidation of the unsaturated diol (42).- The diol (42) (20 mg.) was stirred with a slurry of manganese dioxide (500 mg.) in chloroform (10 ml.) overnight. The solution was filtered and the solvent removed under vacuum furnishing the hydroxy enone (43) (19 mg.) which was crystallised from pentane, m.p. 128-129.5°: n.m.r., q at τ 2.98 (1H-15; $J = 10\text{c./sec.}, 2\text{c./sec.}$); d at τ 3.85 (1H-16; $J = 10\text{c./sec.}$): i.r., ν_{\max} .

3520, 3035, 1685 cm^{-1} : u.v., 238 μ ($\log \epsilon=3.8$).
 (Found: C, 79.3; H, 10.2. $\text{C}_{20}\text{H}_{30}\text{O}_2$ requires C, 79.4;
 H, 10.0%).

Dihydroerthroxylool B (44, R=OH).- Erythroxylool B
 (31, R=OH) (500 mg.) in ethyl acetate (10 ml.) was
 hydrogenated over Pd./C catalyst. Filtration,
 removal of the solvent and crystallisation of the
 residue from methanol gave dihydroerythroxylool B
 (44, R=OH) (462 mg.) m.p. 128-129° (lit.²⁷ m.p. 128-130°).

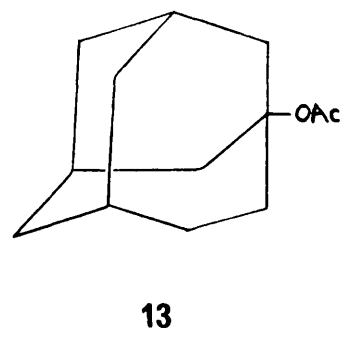
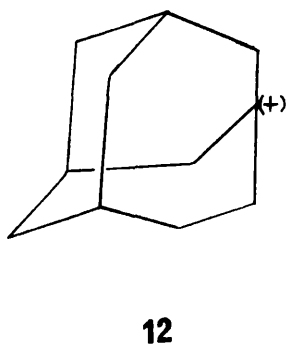
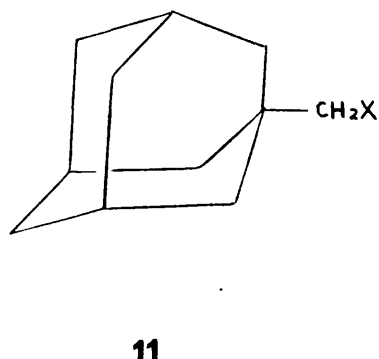
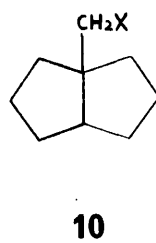
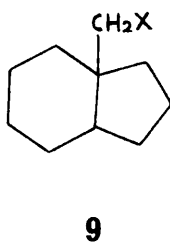
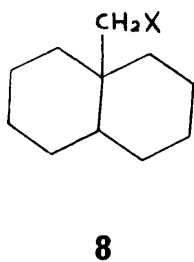
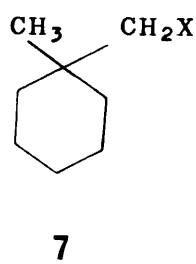
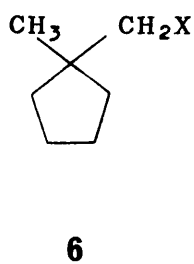
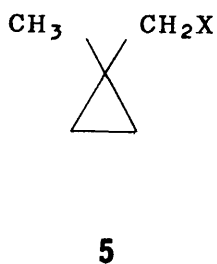
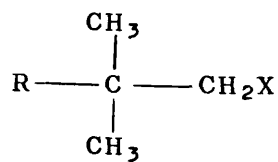
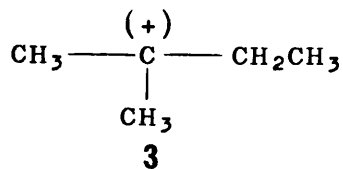
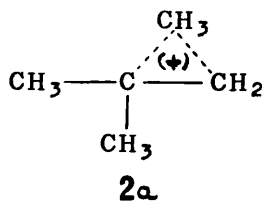
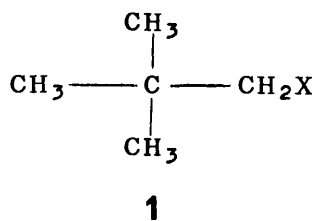
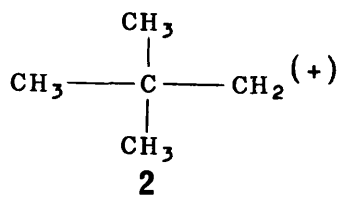
Dihydroerythroxylool B acetate (44, R=OAc).- The alcohol
 (44, R=OH) (45 mg.) was converted to the acetate by
 reaction with acetic anhydride in pyridine. Workup
 furnished an oil which was purified by distillation to
 yield dihydroerythroxylool B acetate (44, R=OAc) (38 mg.):
 i.r., ν_{max} . 1725 1245 cm^{-1} .

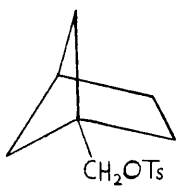
Dihydroerythroxylool B tosylate (44, R=OTS).- Dihydro-
 erythroxylool B (44, R=OH) (310 mg.) was reacted with
 toluene-p-sulphonyl chloride (514 mg.) as described
 above for the tosylation of erythroxylool B. Dihydro-

erythroxylo1 B tosylate (44, R=OTs) (325 mg.),
 m.p. 128-129°, was obtained by crystallisation of
 the crude product from methanol: n.m.r., \underline{S} at
 τ 6.20 (2H-17); \underline{S} at τ 7.55 (3H-aromatic methyl);
 \underline{q} at τ 2.40 (4H-aromatic H's). (Found: C, 73.0;
 H, 9.2. $C_{27}H_{40}O_3S$ requires C, 72.9; H, 9.1%).

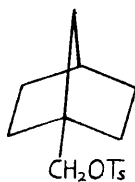
Acetolysis of dihydroerythroxylo1 B tosylate (44, R=OTs).-

Dihydroerythroxylo1 B tosylate (44, R=OTs) (83 mg.)
 was treated for 24hr. with refluxing acetic acid
 containing sodium acetate (111 mg.) as a buffer.
 Workup afforded a residue (55 mg.) consisting of two
 acetates (55 and 45%) (g.l.c. 1% S.E.30 at 175°).
 These products were identical (g.c.m.s.) to the
 acetates derived from hydrogenation of the products
 from the acetolysis of erythroxylo1 B tosylate, i.e.
 (34 and 39, R=OAc).

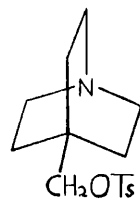




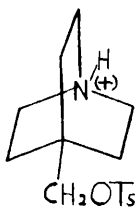
14



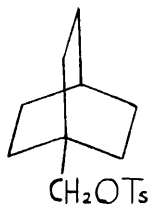
15



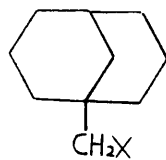
17



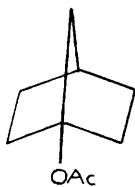
18



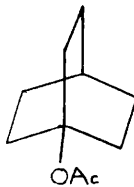
16



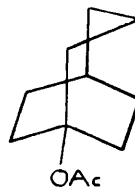
19



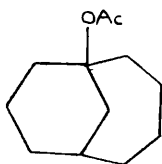
20



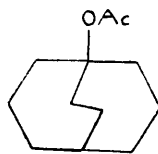
21



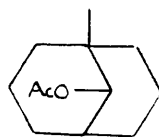
22



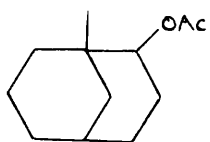
23



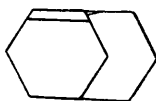
24



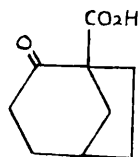
25



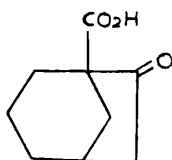
26



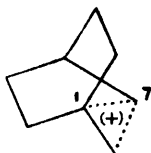
27



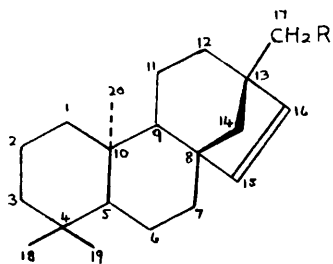
28



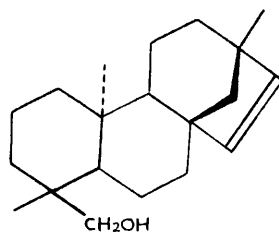
29



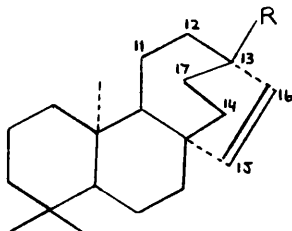
30



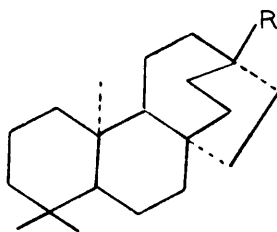
31



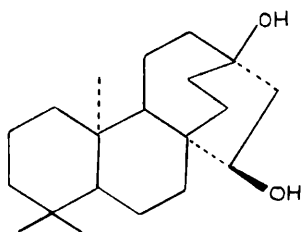
32



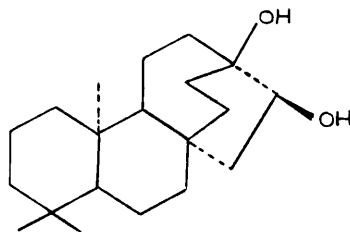
33



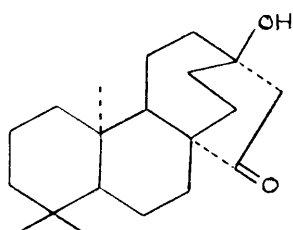
34



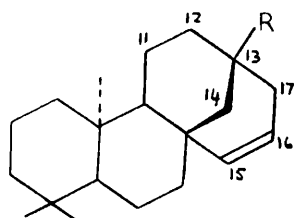
35



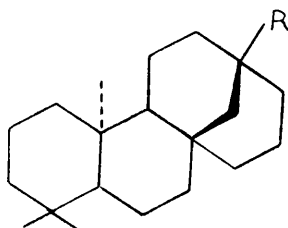
36



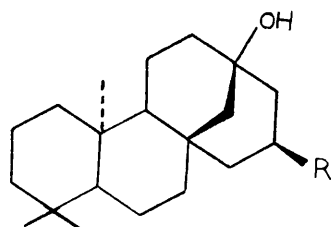
37



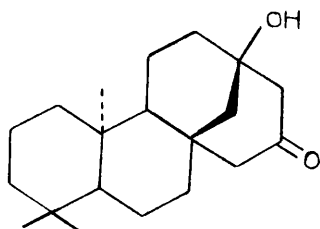
38



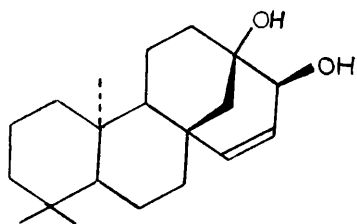
39



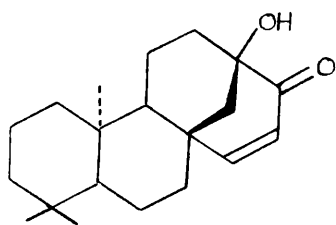
40



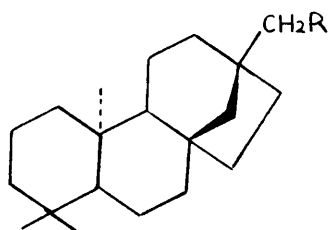
41



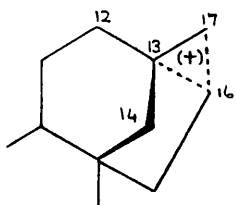
42



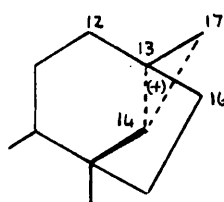
43



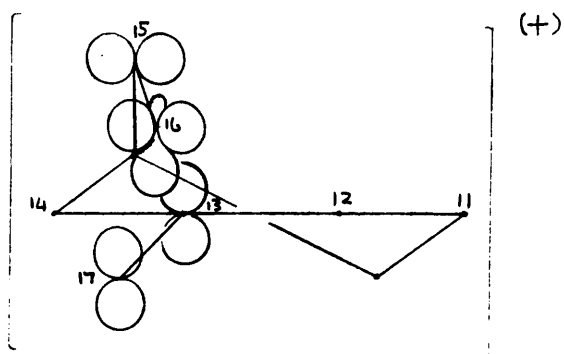
44



45



46



47

Acid catalysed rearrangements of tetracyclic diterpenes.

Wenkert⁴⁰ has suggested that tetracyclic diterpenes may derive from the tricyclic precursors of the pimaradiene type by protonation and cyclisation to intermediates of the form (48). This is in effect a face-protonated cyclopropyl cation⁴¹, opening of which would yield the various tetracyclic diterpenes and proton loss from which would give the known pentacyclic diterpene trachylobane (49). This suggestion stimulated Appleton et. al.⁴² to seek in vitro conditions which would convert any one of these diterpenes into an equilibrium mixture containing other members of the same series through a hydrogen-bridged ion (48)(or equivalent). Table 1. summarises the results of treating these diterpenes with hydrochloric acid in chloroform for various time intervals.

Particularly interesting was the conversion of stachene (50) into iso-atisirine and atisirine (52). The face-protonated cyclopropyl cationic species was discounted as the sole product forming intermediate in this rearrangement since the (iso) atisirine: (iso) kaurene

Table 1.

Product composition after acid treatment

Hydrocarbon	Reaction time		Product composition (%)		
	a	b		a	b
Stachene (50)	4 days	21 days	Stachene	44	35
			(iso)-Kaurene	44	51
			(iso)-Atisirene	12	14
Kaurene (51)	2 hr.	14 days	(iso) Kaurene	100	94
			(iso) Atisirene	-	6
Isoatisirine (52)	2 hr.	14 days	(iso) Kaurene	-	0.5
			(iso) Atisirine	100	99
Trachylobane (49)	15 min	14 days	Kaurene	1	1
			isoKaurene	3	3
			isoAtisirine	90	90
			Atisirine	6	6

product ratio differed substantially depending on whether it was derived from stachene (50) or trachylobane (49), and so it was suggested that the stachene \rightarrow iso-atisirine/atisirine rearrangement could be rationalised by invoking a hydride shift from C-12 to C-16 followed by a Wagner-Meerwein rearrangement of the ethane-bridge to C-12 (i.e. part structures 53 \rightarrow 54 \rightarrow 55). This appeared feasible as it would involve the transfer of the positive charge from a five-membered ring to an energetically more favourable site in a six-membered ring where smaller angle strain is involved⁴³.

From these results it appeared that the in vitro interconversion of the members of the series is possible, however, under the conditions employed, the rate of this interconversion between certain of the skeletal types was so slow as to preclude the ready attainment of equilibrium. The products obtained under these reaction conditions presumably depend largely on the relative stability of the carbonium ion from which they derive. This explains the absence of stachene (50) from the rearrangements of kaurene (51), isoatisirine (52) and

trachylobane (49) as it would be formed via a secondary carbonium ion whereas iso(kaurene) and iso(atisirine) are derived from a tertiary carbonium ion.

Accordingly, in an effort to shed more light on these reactions, it was decided to react certain of these olefinic hydrocarbons with acid under more drastic conditions which might allow the attainment of a thermodynamic equilibrium of products.

Small samples of kaurene (51) were treated with hot formic acid for time intervals ranging from 30 minutes to 2 days. Analyses of the products by g.l.c. and t.l.c. indicated that the major reaction products after 30 minutes were formates but that with time these were eventually completely converted into hydrocarbons.

To establish the structures of these products a larger quantity of kaurene was reacted in hot formic acid for 30 minutes and the resulting formates isolated. Reduction of this mixture by lithium aluminium hydride in diethyl ether followed by separation by preparative thin layer chromatography afforded three alcohols in a yield of 20, 25 and 50%. Formylation of the mixture of these alcohols regenerated the original formates showing that no rearrangement had occurred during the reduction.

The n.m.r. spectra of the three alcohols indicate the secondary nature of the functional group and the presence of four tertiary methyl groups in each case.

The carbinol proton in the least polar alcohol (56, R=OH) (20% of total product) m.p. 93-95°, resonates as a quartet at τ 5.80. Double irradiation experiments demonstrated the coupling of this proton to its two neighbours at C-16, one at about τ 8.76 ($J=3\text{c./sec.}$) and the other at τ 8.10 ($J=6\text{c./sec.}$). In the reverse experiment the proton at τ 8.10 was sharpened from a multiplet to a doublet ($J=12\text{c./sec.}$). The protons of the methylene groups are magnetically distinct because of the shielding effect of the hydroxy function on the eclipsing proton. This is substantiated by the fact that the methylene proton at higher field has a spin-spin coupling constant of 3 c./sec. with the carbinol proton whereas the value for the lower-field proton is 6 c./sec. In a five-membered ring the relevant dihedral angles are respectively 120° and 0°.

Oxidation of this alcohol (56, R=OH) with Jones' reagent furnished the ketone (57) m.p. 86-88°, which exhibits carbonyl absorption in the infra-red at 1736 cm^{-1} indicating the presence of a carbonyl group in a cyclopentane ring.

The most polar alcohol (58, R=OH) m.p. 103-104°, displays a broad doublet at τ 5.38 due to the single carbinol proton at C-16 and a quartet at τ 6.44 which also integrates for one proton, being the lower-field proton of the methylene group at C-15. By spin-decoupling experiments it was shown that the proton τ 6.44. has a coupling of 6c./sec. with the carbinol proton and a coupling of 14c./sec. with its geminal neighbour at τ 8.90. The carbinol proton has a coupling of 3-4 c./sec. with this higher field proton and no other coupling.

Oxidation of this alcohol (58, R=OH) gave a ketone (59), m.p. 100 - 102°, which has a carbonyl frequency of 1742 cm^{-1} confirming that this is also a cyclopentanone.

A decision as to which ketone has the carbonyl group at C-15 and which at C-16 was made by a study of the changes in chemical shift of the methyl groups of the ketones induced by changing the solvent from deuteriochloroform to benzene. It has been shown^{44,45} that any methyl group which lies in front of a plane

drawn through the carbon of the carbonyl group and at right angles to the C-O bond, exhibits a negative (i.e. downfield) shift, while methyl groups on the other side of the plane suffer an upfield shift. This is thought to occur because the benzene molecule forms a short-lived collision complex with the polarised carbonyl group in such a way as to maximise the attraction between the π -electrons of the aromatic ring and the positive carbon of the carbonyl and at the same time to minimise the repulsion with the negative end of the dipole. This is best satisfied if the benzene molecule complexes behind the carbon of the carbonyl, away from the oxygen thus shielding any methyl group behind the plane of the carbonyl and deshielding a methyl in front of this plane.

It can be seen that the C-17 methyl group in (59) is close to, but in front of, the plane drawn through the carbon of the carbonyl. Therefore, if the assignment is correct, a -ve solvent shift should be observed for this methyl. This is indeed the case ($\Delta\gamma = -0.05$). The solvent shift for the corresponding methyl in (57) is $\Delta\gamma = +0.10$ thus confirming the structures of these two ketones.

The alcohols (56 and 58, R=OH) have been prepared by Suhk-Dev⁴⁶ by hydroboration of stachene, and a comparison of the physical and spectral properties of these and the derived ketones⁴⁷, with the compounds formed by the action of formic acid on kaurene substantiated our assignment of the structures of the latter series.

The alcohol of intermediate polarity (60, R=OH) (25% of total product) is probably also a substituted stachane since it has four tertiary C-methyl groups. The carbinol proton at C-12 resonates as a broad singlet with a half band width of 6c./sec. at τ 6.56 in its n.m.r. spectrum. Irradiation in the methylene region at τ 8.50 collapsed this to a sharp singlet.

The stereochemistry of the hydroxy function in (60, R=OH) is open to conjecture. If, as seems likely, ring C is in a chair conformation⁴⁸, the hydroxy group must be exo thus giving a dihedral angle of 60° between the carbinol proton and both protons of the adjacent methylene group, and so accounting for the small spin-spin coupling of the carbinol proton in the n.m.r. spectrum of the alcohol. Conversely, if ring C is in the boat conformation the hydroxyl function must be endo.

Oxidation of this alcohol (60, R=OH) yielded the ketone (61) m.p. 86 - 88° with V_{\max} 1710 cm^{-1} indicating a cyclohexanone. This ketone exhibits the expected downfield shift in the n.m.r. signal of the C-17 methyl group on going from deuteriochloroform to benzene as solvent ($\Delta\tau = -0.10$) due to the location of the carbonyl function.

Ourisson⁴⁹ has isolated the acetate (60, R=OAc) from acetic acid catalysed ring opening of trachylobane (49), and thus the structures assigned to (60, R=OH), (60, R=OAc) and (61) were confirmed by comparison of their physical and spectral properties with those reported.

The hydrocarbons which were produced by prolonged treatment of kaurene with formic acid were chromatographed by t.l.c. over silver nitrate-silica gel. The individual fractions were then analysed by G.C.M.S. to allow structure assignments to the products, the bulk of which were tetracyclic diterpenes. The most abundant were stachene (50), isokaurene (51) and isoatisirine (52), however the exact proportion of these could not be determined because of the method of analysis.

The prolonged reaction of formic acid with stachene (50) produced a mixture of hydrocarbons identical (g.l.c.) to that obtained from kaurene, thus suggesting that these processes are attaining thermodynamic equilibrium.

The formation of secondary formates by the reaction of hot formic acid with kaurene for a short time, indicates that the controlling factor in this case is more likely to be the stability of the products rather than the stability of the carbonium ion intermediates as in the case of treatment with hydrochloric acid in chloroform.

Protonation of kaurene followed by Wagner-Meerwein rearrangement will lead to the cation (53), solvent capture from the least hindered side of the ion yielding (58). The other cyclopentyl substituted product (56) could arise either from hydride shift from C-15 to C-16 followed by solvent capture or possibly by proton loss in the cation yielding stachene (50) which would then form a mixture of (56 and 58, R=OF) by formic acid addition across the double bond.

The product (60, R=OF) is the most interesting as this represents a solvent capture of the cation formed by the formal hydride shift invoked⁴² in the conversion of stachene \longrightarrow (iso) atisirine (54). It is noteworthy that although the stereochemistry of the functional group in (60) can not be unequivocally determined solvent capture is stereospecific, suggesting the intermediacy of 'non-classical (or equivalent) species.

Experimental.

Formic acid treatment of Kaurene - Kaurene (1 g.) was dissolved in a minimum amount of chloroform and added to formic acid (80 ml.). After heating the mixture for 30 min. at 90°C the formic acid was removed under vacuum, leaving a residue (1.1 g.) which t.l.c. and g.l.c. analyses indicated to be mainly formates.

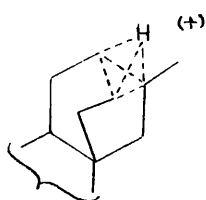
Hydride reduction of the mixed formates - The crude mixture of formate products (1.g.) was treated with excess lithium aluminium hydride in refluxing diethyl ether for 2 hr. Saturated sodium sulphate was then added, followed by anhydrous sodium sulphate. The solution was filtered and the ether removed to give a mixture of alcohols (850 mg.) which was separated into the individual components by preparative t.l.c.

The least polar component (56, R=OH) (20% of total alcohol product) had m.p. 93-95° (lit.⁴⁶ m.p. 96-97°): n.m.r. q at τ 5.80 (1H-15, J = 6c./sec., 3c./sec.): q at τ 8.10 (1H-16, J = 6c./sec., 12c./sec.); s at τ 9.06, 9.08, 9.16, 9.21 (all 3H-methyls).

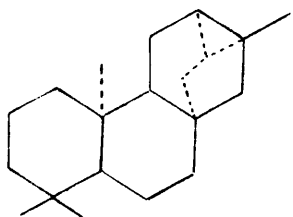
Oxidation of this alcohol (56, R=OH) by Jones reagent in the normal manner yielded the ketone (57) which had m.p. 86-88° (lit.⁴⁷ m.p. 88-89°): n.m.r., s at τ 9.00, 9.19, 9.21, 9.24 (all 3H-methyls): n.m.r. in benzene s at τ 9.08 (3H-methyl), s at τ 9.15 (6H-two methyls), s at τ 9.22 (3H-methyl): i.r. ν_{\max} . 1736 cm^{-1} .

The most polar component (58, R=OH) (55% of total alcohol product) had m.p. 103-104° (lit.⁴⁶ m.p. 104-105°): n.m.r., b.d. at τ 5.38 (1H-16, J = 6c./sec.); q at τ 6.44 (1H-15, J = 6c./sec., 14c./sec.); s at τ 9.10, 9.13, 9.18, 9.22 (all 3H-methyls).

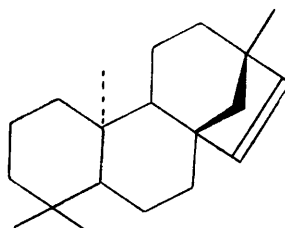
Oxidation of this alcohol (58, R=OH) furnished the ketone (59) m.p. 100-102° (lit.⁴⁷ m.p. 102-103°): n.m.r. s at τ 9.04, 9.19 (both 3H-methyls) s at τ 9.15 (6H-two methyls): n.m.r. in benzene s at τ 9.00, 9.16, 9.25, 9.34 (all 3H-methyls): i.r. ν_{\max} . 1742 cm^{-1} .



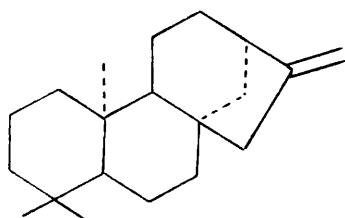
48



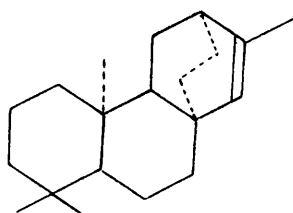
49



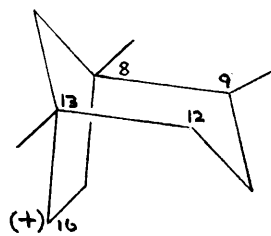
50



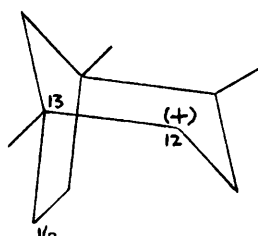
51



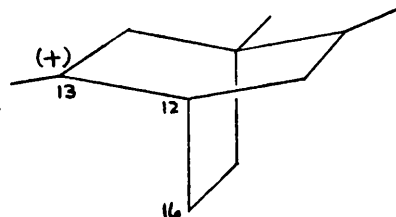
52



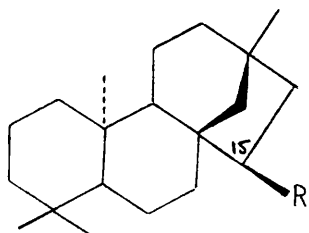
53



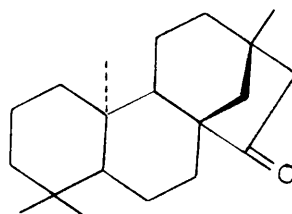
54



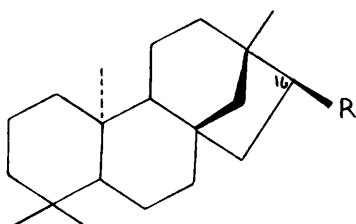
55



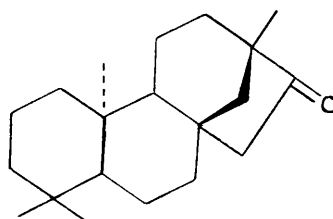
56



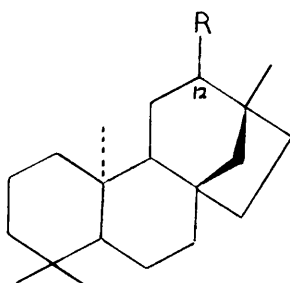
57



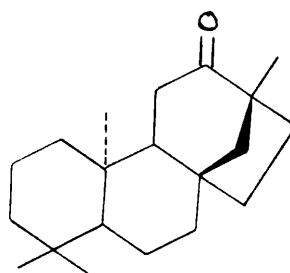
58



59



60



61

Hydride Shifts in Bicyclic Systems

Winstein and Trifan^{50,51} observed that the rate of solvolysis of resolved exo-norbornyl tosylate (62, R=OTs) is 350 times greater than that of its endo isomer (63, R=OTs) and that the sole product is the racemic exo-acetate (62, R=OAc). This led them to suggest that the intermediate is a bridged ion (64) formed by delocalisation of the C-1, C-6 σ bond. They conceded that at least three alternatives to the symmetrical bridged ion would convert a classical norbornyl cation into its enantiomer. (a) A Wagner-Meerwein migration of C-6 from C-1 to C-2, (b) a 1,3-hydride shift from C-6 to C-2 or (c) a hydride shift from C-3 to C-2. The intermediacy of ion (64) is the most attractive explanation as it accounts for the exclusive formation of exo-substituted products and also as the C-6, C-1 bond is trans-anti-parallel to the departing exo-tosylate group anchimeric assistance by this bond would account for the large rate enhancement found in the exo over the endo- tosylate.

This type of bridged cation had also been suggested⁵² as an intermediate (67) in the rearrangement of camphene hydrochloride (65) to isobonyl chloride (66).

This interpretation cannot, however, be distinguished from one in which there are three classical ion intermediates (68, 69 and 70^x) which are rapidly interconvertible⁵³. The postulation of a bridged 'nonclassical ion' is conceptually simpler and more economical, and shall therefore be used in this discussion.

An attempt was made by Roberts, Lee and Saunders^{54,55} to determine if a symmetrical intermediate such as (64) is involved in the solvolysis of norbornyl derivatives (62) or whether the alternatives conceded by Winstein ((a) (b) and (c)) are important. If (64) is the sole product-forming intermediate, then during the solvolysis of norbornyl derivatives labelled by ¹⁴C at C-2 and C-3 the radioactivity should be scattered evenly over positions 1,2,3 and 7 in the norbornyl skeleton.

x

See Chapter 4.

The results demonstrated that rearrangement did occur but that it was somewhat more extensive than the simple reactions involving (64) would predict. In particular, during the acetolysis of the exo-norbornyl brosylate, some 15 per cent of the radioactivity found its way to positions 5 and 6, establishing beyond question that $6 \longrightarrow 2$ hydrogen migrations do occur to a significant extent during this reaction. To account for the observed ^{14}C distribution Roberts suggested that another ion (71), the nortricyclonium ion, is formed in competition with the formation of (64). This nortricyclonium ion has a three fold axis of symmetry in which carbon atoms 1,2 and 6 are totally equivalent. Nucleophilic attack by solvent at any of these positions leads to racemic exo-2-norbornyl acetate (62, $\text{R}=\text{OAc}$). The isotope distribution can be accounted for if 55 per cent of the reaction proceeds via ion (64) and 45 per cent via ion (71).

Whereas Roberts regarded (71) as discrete intermediate Winstein has suggested an alternative representation⁵⁶ wherein the ^{14}C scrambling arises from the interconversion of the three bridged ions (64, 64a and 64b) by means of $6 \longrightarrow 2$ and $6 \longrightarrow 1$ hydride shifts. The consequences of

two hypotheses are similar but in Winstein's interpretation the ion (71) is regarded as a transition state between the bridged ions rather than a discrete intermediate. In other words according to Winstein the ion (71) would constitute a maximum in the energy profile of the norbornyl 'non-classical' ion whereas Roberts considers it to be a minimum in the energy profile of a distinct process.

The direct observation of the norbornyl cation by the technique of nuclear magnetic resonance⁵⁷ has shed some light on its structure. The n.m.r. spectrum of the antimony hexafluoride salt of the cation at -23°C shows all the protons to be equivalent while at -120°C the protons are resolved into three peaks of relative areas 4:1:6. The high-temperature spectrum is taken to indicate time-average equivalence of all protons in the 2-norbornyl cation. Such equivalence is possible only if three events are occurring rapidly and simultaneously: (1) the formation of the bridged ion (64); (2) 6 \rightarrow 2 hydride shift; and (3) 3 \rightarrow 2 hydride shift. The low-temperature spectrum is postulated to arise from a

'freezing-out' of the third of these processes, viz. the $3 \rightarrow 2$ hydride shifts. From the temperature-dependence of the spectrum the rate constant for the $3 \rightarrow 2$ hydride migrations can be determined⁵⁸. Thus, at low temperatures the first two processes are still operating and this results in three sets of magnetically distinct protons: the four protons bonded to C-1, C-2 and C-6; the single proton at C-4; and the six protons at C-3, C-5 and C-7. The fact that $6 \rightarrow 2$ hydride migrations cannot be 'frozen-out' indicates that these are fast and facile processes which must be important in all reactions involving bicyclo [2,2,1] heptyl cations.

This type of $6 \rightarrow 2$ hydride shift is apparent in the rearrangements of the fenchyl series⁵⁹. Fenchol (72) is dehydrated by potassium bisulphate to a mixture of α , β and γ -fenchenes (73, 74, 75) and cyclofenchene (76). α -Fenchene is the product of normal Wagner-Meerwein rearrangement, but β and γ fenchenes

are products of formal 6,2 hydrogen shifts and Wagner-Meerwein rearrangements and cannot be derived from fenchol by any reasonable combination of 1,2 carbon and hydrogen shifts. Although cyclofenchene (76) is converted by potassium bisulphate to a mixture of (74) and (75)⁶⁰, deuterium labelling experiments have demonstrated that it cannot be an important intermediate in the rearrangement.

As would be expected from the n.m.r. study of the 2-norbornyl cation, hydrogen shift from C-3 to C-2 appears to be the least important rearrangement process in this system. Together with Wagner-Meerwein rearrangements and 6,2 shifts it would lead to radioactivity being found at C-4 in the product from solvolysis of norbornyl derivatives labelled at C-2 and C-3 by ¹⁴C. Roberts⁵⁵ has cogently argued that there is no activity at this position and that hence there is no 3,2 hydride shift during the acetolysis of exo-norbornyl tosylate (62, R=OTS). However, Dills⁶¹ has demonstrated that under formolysis conditions the isotopic labelling cannot be accounted for solely on the basis of the skeletal

rearrangement implied by (64) and (71) and has calculated the extent to which 3,2 hydride shifts must occur to give a quantitative explanation of the results.

More obvious evidence for the existence of 3,2 hydride shifts has been obtained by a study of the acetolyses of exo and endo-2-t-2-norbornyl brosylates⁶².

Table 2.

	C ₂	C ₃	C _{1,4,7}	C _{5,6}
<u>exo</u> -OBS	35	2	36	27
<u>endo</u> -OBS	38	1	36	25

The scrambling which was estimated by degradation is shown above (table 2) and the activities detected at C-3 indicated small amounts of a net 3,2 hydride shift. It can be seen that these hydride shifts are much less important in these systems than the facile 6,2 hydride shift.

The timing of Wagner-Meerwein and 6,2 shifts have been considered. The 6,2 hydrogen shift in the solvolysis of exo-norbornyl brosylate (62, R=OBS) decreases in importance in a more nucleophilic medium, namely aqueous acetone, and Winstein⁵¹ has deduced from this information that hydride shifts in the norbornyl cation do not accompany the formation of the bridged ion (64) but occur as a subsequent step. Further evidence supporting this has been obtained from a study of the acetolyses of apoisobornyl brosylate (77, R=OBS) and exo-camphenilyl brosylate⁶³ (78, R=OBS). These compounds yield an identical mixture, 49 per cent of which consists of β -fenchoisocamphoryl acetate (79, R=OAC) arising from a 6,2 hydride shift. In a more nucleophilic solvent the yield of (79) is diminished. The identical yield of (79) from (77, R=OBS) and (78, R=OBS) is significant as ionisation of (77) and (78) leads to the same bridged ion (80) and would seem to indicate that (80) is formed before hydride shift occurs forming ion (81), which then undergoes acetate capture yielding (79, R=OAc).

Although the occurrence of 6,2 hydrogen shifts in the norbornyl system has been well established for some time, the mode of transfer of the hydrogen has been an object of conjecture. These hydride transfers have been formulated as proceeding via either face-protonated cyclopropyl intermediates, e.g. (71) or edge protonated cyclopropyl transition states such as ion (82)⁵¹. The essential difference between (71) and (82) lies in symmetry properties. Thus, in the collapse of the nortricyclonium ion (71) to ion (64, 64a and 64b), the hydrogen that lies in the three fold axis cannot show preferences for attachment to either side of any of the carbon atoms surrounding the axis. As a result the endo-exo distinction of the hydrogen is lost. This is not the case with the edge protonated ion (82) and Berson⁶⁴ has used this difference as the basis of an experimental distinction between the two intermediates. He has shown that in the 2 carboxy-3-methyl-5-norbornyl cation the intramolecular hydride shift is exclusively endo \longrightarrow endo

Using the deuterium labelled compound (83) he finds that the deuterium is exclusively in position 2 in the rearranged lactone (85). This is inexplicable by any mechanism involving a transient nortricyclonium type ion and indicates that in this, albeit special, case the hydride shift is stereospecific via an edge protonated cyclopropyl cation.

A similar result has been found in the rearrangement of 2-phenylnorbornane-2,3-cis-exo-diol-5,6- d_2 (86, R=OH)⁶⁵ which proceeds with intramolecular migration⁶⁶ to give the product (89). At least 94% of the deuterium originally in the exo position of (86) resides in the exo-5-position of (89) arising by discrete stereospecific shift of the exo-6-deuterium via the bridged intermediates (87). The same workers⁶⁷ have recorded stereospecific hydride shifts in the solvolysis of (86, R=OTS).

Nearly all the recorded hydride shifts in bicyclic systems occur in bicyclo (2,2,1) heptyl compounds, however a somewhat different type of hydride shift has been observed in the bicyclo (3,3,1) nonyl system. The reaction

of formic acid on bicyclo (3,3,1) nonan-2 β , 3 β -oxide (90, R=H)^{68,69} produces a mixture of alcohols the major components of which are (91, R=H) and (92, R=H) resulting from a hydride shift from C-7 to C-3 in the bicyclononyl skeleton. Similarly 7 β -methyl-bicyclo (3,3,1) nonan-2 β ,3 β -oxide (90, R=Me) forms (91, R=Me) or (92, R=Me) under the same conditions. This type of 1:5 hydride shift is probably akin to those found in medium-sized rings. In the known double-chair conformation⁷⁰ of the bicyclo (3,3,1) nonyl system the hydrogens at C-3 and C-7 are in close proximity resulting in steric strain which probably facilitates the trans-annular hydride shift.

The solvolytic behaviour of *exo* and *endo*-bicyclo (3,2,1)octane-6-Toluene-p-sulphates.

Although there is ample evidence of 1:3-hydride shifts as invoked in the interconversion of tetracyclic diterpenes (Chapter 2), occurring in the bicyclo(2,2,1) heptane series (*vide supra*) at the time the present investigation was initiated, there was no recorded case of the corresponding effect (*i.e.* a 4:6 - shift) in the simple bicyclo (3,2,1) octane system. Accordingly the solvolytic behaviour of *exo*- and *endo*-6-substituted-bicyclo (3,2,1) octanes (93 and 94, R=OTS) was examined particularly from the standpoint of determining the nature of the kinetically - controlled products.

3-Bromobicyclo (3,2,1) oct-3-en-6-yl formate⁷¹ was prepared by the addition of dibromocarbene to norbornadiene followed by lithium aluminium hydride reduction and addition of formic acid across the $\Delta^{6,7}$ double bond. Catalytic hydrogenation in basic solution then gave a mixture of the *exo*- and *endo*-bicyclo (3,2,1)

octan-6-ols (in the ratio of 25:1) which was readily separated by preparative thin-layer chromatography or, more conveniently, by fractional crystallisation from n-pentane. In the ^1H n.m.r. spectrum of the more abundant isomer, m.p. $143\text{--}144^\circ$, the carbinyl proton at C-6 appeared as a broadened doublet at τ 5.70 ($J = 7\text{c./sec.}$), whereas the corresponding proton in the spectrum of the other alcohol, m.p. $192\text{--}194^\circ$, appeared at τ 5.50 ($W^{1/2} = 22\text{c./sec.}$). The difference in half band width is due to the spin-spin coupling which is larger for the endo than exo isomer of the proton at C-5. An examination of models shows that the relevant dihedral angles between the C-5 and C-6 protons is approximately 40° in the endo- and 90° in the exo- isomer.

Oxidation of both isomers gave the same ketone⁷¹ (95) which on lithium aluminium hydride reduction was converted predominantly into the alcohol, m.p. 192° . The above spectral and chemical evidence is compatible with stereoformulae (93, $\text{R}=\text{OH}$) and (94, $\text{R}=\text{OH}$) for the alcohols m.p. 143° and 192° respectively.




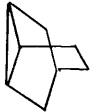


The corresponding toluene-p-sulphonates (93 and 94, R=OTs) were then prepared, individually subjected to buffered acetolysis in sealed ampoules at 105° for 100 half-lives, and the nature and distribution of the products determined (see Tables 3 and 4). The olefinic products were readily analysed by gas-liquid chromatography (g.l.c.) whereas the composition of the acetate fraction was determined by high-resolution n.m.r. spectroscopy at 100 Mc./sec. in the 8 τ region. This was facilitated by the fact that acetate methyls of all the possible products were magnetically non-equivalent (see Table 6.) Synthetic mixtures were used to confirm the product assignments and the compositions of the acetate mixtures were evaluated from peak areas and peak heights. A complete separation by g.l.c. of the acetates (or corresponding alcohols) formed in these solvolyses was not realised, nevertheless, the results of a partial g.l.c. separation reinforced the conclusions as to product distribution based on n.m.r. data.

The relevant bicyclo (3,2,1)-; bicyclo (2,2,2)- and tricyclo (3,2,1,0²⁷)-octyl derivatives required for comparison purposes were prepared by well-established procedures. Thus, Diels-Alder addition of vinyl acetate to cyclohexadiene⁷⁵ followed by reduction led to the bicyclo (2,2,2) derivatives (101) and Wolf-Kischner reduction of the semicarbazone of bicyclo (2,2,2) octenone furnished bicyclo (2,2,2) oct-2-ene (98). Bicyclo (3,2,1) oct-6-ene (96) was conveniently obtained by treating exo-6-bicyclo (3,2,1) octyl tosylate (93, R=OTs) with refluxing collidine. All of the standards were stable to the reaction conditions.

The first feature which emerges from a consideration of Tables 3 and 4 is the large amount of exo-2-bicyclo (3,2,1)- and 2-bicyclo (2,2,2) octyl acetates (100 and 101, R=OAc) produced from the acetolysis of (93, R=OTs). Normal Wagner-Meerwein rearrangement of the cation (104) would only lead to 6-substituted bicyclo (3,2,1) octyl derivatives. These other products can be explained formally by either (a) a 4:6- hydride shift in the classical cation leading to (105) and thence by Wagner-Meerwein rearrangement to (106) or (b) the formation of tricyclo

Table 3.







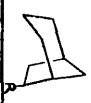

Olefins[Ⓢ] produced from buffered acetolysis of (93 and 94 R=OTs)

Tosylate	Ref.87  (96)	Ref.88  (97)	Ref.89  (98)	Ref.90  (99)
(93, R=OTs) 	100%	-	-	-
(94, R=OTs) 	60%	40%	-	-

[Ⓢ]Compounds 96, 97 and 98 were stable to the buffered acetolysis conditions.

Table 4.

Acetates* formed from buffered acetolysis of (93, R=OTs),
(94, R=OTs) and (99)

Tosylate	 (93, R=OAc)	 (94, R=OAc)	Ref. 91  (100, R=OAc)	Ref. 91  (101, R=OAc)	Ref. 91  (102, R=OAc)
93, R=OTs 	16%	0	40%	44%	< 1%
94, R=OTs 	60%	0	19%	21%	0
(99) 	26%	0	33%	35%	6%

* All these acetates were stable to the buffered acetolysis conditions.

(3,2,1,0^{2,7}) octane (99) by proton loss from (104) followed by acid-catalysed cyclopropane ring-opening to (104), (105) and (106). However, the product distribution obtained from buffered acetolysis of (99) illustrates that this hydrocarbon cannot be the sole intermediate by which (100 and 101, R=OAc) are formed, since this would demand the formation of at least 6% of endo-2-bicyclo (3,2,1)octyl acetate (102, R=OAc). In fact, allowing for a detection limit for (102, R=OAc) of 1%, the mechanism involving tricyclo (3,2,1,0^{2,7}) octane as the key intermediate cannot be operating to an extent of more than 20%. In addition, the lack of a detectable quantity of (102, R=OAc) in comparison to the large amount of (100 and 101, R=OAc) formed is characteristic of the solvolytic behaviour of 2-bicyclo (2,2,2) octyl tosylate (101, R=OTs)^{72,73} exo-2-bicyclo (3,2,1) octyl tosylate (100, R=OTs)^{74,75} and Δ^3 -cyclohexenylethylbrosylate⁷⁶. In other words, the formation of (100 and 101, R=OAc) from (93) R=OTs) would suggest the intermediacy of the non- classical species (108) or a rapidly equilibrating pair of the corresponding classical cations. In the ensuing discussion

non-classical species are used for convenience and do not rule out in each case the possibility of equilibrating classical ions¹⁷.

When this proposal is taken in conjunction with the formation of unrearranged acetate (93, R=OAc) of retained stereochemistry from (93, R=OTs), itself suggestive of a mesomeric 6-cation (107), the mechanistic scheme shown in figure 1. can be formulated as the major product-forming pathway for the solvolysis of (93, R=OTs).

Ionisation of (93, R=OTs) with participation of the C-4 - C-5 sigma-bond will lead to the non-classical ion (107) which can either (a) suffer solvent capture at C-5 or C-6 (these positions are equivalent) to give the exo-6-acetate (93, R=OAc) or (b) undergo 4:6-(or 4:5-) hydride shift leading to the bridged species (108) from which (100 and 101, R=OAc) are readily formed. Solvent capture at C-4 in (108) would lead to the exo-2-bicyclo (3,2,1) octyl derivative (100, R=OAc) and capture at C-5 to the bicyclo (2,2,2) octyl derivative (101, R=OAc). It would appear from Table 4 that hydride shift is extremely

competitive with counter-ion capture and this may be due to the greater overall strain and larger number of non-bonded interactions associated with (107) compared with (108) as becomes apparent from an examination of molecular models.

It can also be seen from a model of (107)⁷⁸ that in the most favourable arrangement for overlap of the p-orbital at C-4 with the π -orbitals at C-5 and C-6, the two C-4 hydrogen atoms are not equivalent (cf. the C-6 protons in the 2-bicyclo (2,2,1) heptyl non-classical ion). However a simple conformational flip of the C-2 to C-4 chain produces the enantiomeric structure in which the relative positions of the C-4 protons are reversed. Hence this proposed conformational equilibrium serves to make both C-4 protons favourably situated to play a part in the theoretically favourable 'edge-protonated' cyclopropane species^{79,51,63} which is consistent with the known stereospecificity of a 6:2-hydride shift in the related bicyclo (2,2,1) heptyl system (see introduction). Hence the 4:6 and 4:5-hydride shifts become equally probable.

By this pathway it is predicted that solvolysis of resolved exo-6-bicyclo (3,2,1) octyl tosylate would lead exclusively to racemic products as the ion (107) is symmetrical and hydride shift from the C-4 position to C-6 and C-5 produces carbonium ions which are 'mirror images' of each other.

The solvolysis of endo-6-bicyclo (3,2,1) octyl tosylate (94, R=OTs) gives only (100 and 101, R=OAc) in terms of rearranged products but there is a much higher proportion of 6-acetate (93, R=OAc) all of which is exo although derived from endo-starting material. In this context, it may be that (94, R=OTs) closely parallels endo-2-norbornyl tosylate⁵¹ in its solvolytic behaviour in that formation of the non-classical ion (107) is competitive with SN2 solvolytic displacement of the tosylate from the least hindered, i.e. exo, side (109). This takes place because the C-4 - C-5 sigma bond is not trans-anti-parallel to the ionising C-O bond in the endo isomer.

The solvolysis of (93 and 94, R=OTs) would therefore seem to represent an entry by way of a hydride shift mechanism into the 2-bicyclo (3,2,1)/2-bicyclo(2,2,2)

octyl cationic system which has already been approached by two σ -, π -, π - and one ring expansion route⁸⁰. These four routes are all thought to involve the intermediate cation (108). It is significant that the ratio of exo-2-bicyclo(3,2,1)/2-bicyclo(2,2,2) octyl products is the same in every case, as that from the solvolysis of the 6-bicyclo (3,2,1) octyl tosylates thus confirming that the reactions have a common intermediate cation of the type (108).

About this time in our work, Wiberg⁸¹ reported that solvolysis of exo and endo bicyclo (3,1,1)heptane-6-methyl brosylates also serve as a route to the same system presumably by ring expansion and hydride shift⁸².

An examination of the product composition also confirms that hydride shift must occur after, and not in competition with, the formation of the non-classical ion (107). If hydride shift were to occur in the classical ion (104) then it would be expected that the endo-4-hydrogen would be the migrating atom. This would introduce the possibility of participation by the C-8 - C-5 sigma bond to form the non-classical ion (110). This is the ion proposed as the intermediate during the

solvolysis of endo-2-bicyclo (3,2,1)octyl tosylate (102, R=OTs)⁷⁵ which by solvent capture at C-4 or C-5 leads exclusively to endo-2-bicyclo (3,2,1) octyl acetate (102, R=OAc). As this compound is absent from the products of 6-substituted bicyclo (3,2,1) octyl tosylates, hydride shift in this system must occur after ionisation to the non-classical ion (107).



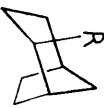





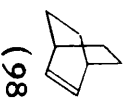

Since our interest in this particular area of carbonium ion chemistry was occasioned by an attempt to interconnect several tetracyclic olefinic diterpenes, we decided to attempt a similar interconversion of bicyclo (3,2,1) oct-6-ene (96), bicyclo (3,2,1) oct-2-ene (97), bicyclo (2,2,2) oct-2-ene (98) and tricyclo (3,2,1,0^{2,7}) octane (99). No acidic conditions could be found which gave hydrocarbon products, addition with or without rearrangement being the main reaction. With hydrochloric acid in chloroform chlorides were formed. Reaction of bicyclo (3,2,1) oct-6-ene (96) with toluene-*p*-sulphonic acid in acetonitrile gave a good yield of exo-6-bicyclo (3,2,1) octyl tosylate

(93, R=OTs). Accordingly the hydrocarbons were treated individually with refluxing acetic acid containing toluene-*p*-sulphonic acid, as a method of analysing the products had been established. The results are shown in Table 5.

These reactions obviously differ markedly from the buffered acetolysis of (93 and 94, R=OTs) in the relatively high yield of endo-2-bicyclo(3,2,1)octyl acetate (102, R=OAc) and the corresponding exo-6-acetate (93, R=OAc)⁸³. This is not unexpected as this reaction is thermodynamically controlled and depends on the stability of the products, unlike the solvolytic reaction which is kinetically controlled and depends on the structure and stability of the intermediates. Accordingly, a high proportion of endo-2-bicyclo (3,2,1)octyl acetate (102, R=OAc), the thermodynamically favoured product⁷⁵ would be expected. It can be seen from Table 5 that all the reactions seem to be attaining, after a time, a thermodynamic equilibrium. A similar result was obtained from formic acid treatment of the hydrocarbons, g.l.c. analyses of the products indicating that similar product distribution had been formed in each case.

Table 5.

Products from treatment of (96), (97), (98) and (99) with HOAc/TsOH

 (93, R=OAc)	 (94, R=OAc)	 (100, R=OAc)	 (101, R=OAc)	 (102, R=OAc)	 (103, R=OAc)
 (96)	0	18%	18%	19%	8%
 (97)	0	25%	22%	27%	12%
 (98)	0	25%	22%	30%	10%
 (99)	15%	23%	21%	30%	11%

Although the formation (see Table 5.) of (93, R=OAc) particularly from (98) and (97) is probably most easily explained by the initial formation of (99) followed by opening of the cyclopropane ring, it does raise the question of whether some of the exo-6-acetate (93, R=OAc) might not arise from a 6:4-hydride shift, i.e. (105) to (104), where (105) would be formed by protonation of (97).

If one considers, as now seems likely, that partial bonding of the type associated with a non-classical species is a necessary criterion for this form of 1:3 hydride shift then a rearrangement of the type (105 \rightarrow (104) would not be expected, for example, from a 2-bicyclo(3,2,1) cation generated from (102, R=OTs). The intermediate formed both from solvolysis of (102) (' σ -route') and Δ^4 -cycloheptenylmethyl brosylate (' π -route')⁸⁴ must have the structure represented by either (110) or the corresponding equilibrating classical cations, hence it is not surprising that no 6:4 hydride shift has been detected since C-6 is not one of the three centres involved (viz. C-1, C-4 and C-5). (In the case of the exo-2-bicyclo(3,2,1)/2-bicyclo(2,2,2) octyl cation C-6 is one of the three atomic centres involved).

In this instance the two C-6 hydrogen atoms are not equivalent in the sense that a 6:5-hydride shift would produce the antipode of (108) whereas the alternative 6:4 shift would reform (107). Berson⁸⁵ has recently produced compelling evidence against a 6:5-hydride shift being involved in the racemisation associated with the solvolysis of optically active (101, R=OTs). However, in terms of a possible 6:4-shift, Walborsky^{72,73} has recorded that the solvolysis of (101, R=OBs) gave (101, R=OAc) 54.1%; (100, R=OAc) 43%; (102, R=OAc) 1.7% and 1.2% of an unidentified component.

In view of this result the solvolysis of 2-bicyclo (2,2,2) octyl tosylate (101, R=OTs) in buffered acetic acid was reexamined. Analysis of the products by (a) n.m.r. examination and g.l.c. of the acetates and (b) g.l.c. of the corresponding alcohols confirmed that the minor, hitherto unidentified, component is indeed, exo-6-bicyclo (3,2,1) octyl acetate (93, R=OAc), possibly arising from 6:4-hydride shift in the ion (108). This result has subsequently been supported by Goering⁸⁶.

It does not appear that the facile hydride shift from C-4 to C-6 in the bicyclo octyl skeleton and the reluctance of the reverse process can be explained in terms of simple angle strain in the classical ions involved. More likely this result reflects the relative stabilities of the two bridged ions (107) and (108) the former probably involving more non-bonded interactions and angle strain than the latter.

Rate studies.

The rates of acetolysis of exo and endo bicyclo (3,2,1) octane-6-toluene-p-sulphonates were determined by the spectrometric method described by Swain and Morgan.³⁷ This utilises the fact that a tosylate function has a higher extinction coefficient at 261 mμ in the ultraviolet than the corresponding anion so that for reactions in transparent solvents rate estimations can be made by measurement of the decrease in optical density of the reaction with time.

The rate constants for the reactions of the exo tosylate at 80° and 100°C and that of the endo tosylate at 80° (Table 7) were determined from a graph of log % unreacted tosylate/time.

Table 7.

exo tosylate	$k^{80^\circ} = 9.8 \times 10^{-5} \text{ sec.}^{-1}$
	$k^{100^\circ} = 6.8 \times 10^{-4} \text{ sec.}^{-1}$
endo tosylate	$k^{80^\circ} = 7.4 \times 10^{-6} \text{ sec.}^{-1}$

These results were highly reproducible being almost identical for several solvolyses. The accuracy of this method in our hands was checked by measuring the rate of acetolysis of cyclohexyl tosylate for which a very good agreement with the literature value was obtained.

Although the difference in reactivity of the *exo* and *endo* tosylate must await a determination of the amount of ion-pair return involved,^{51,74} it is nevertheless interesting to compare the 6-bicyclo (3,2,1) octyl system with the norbornyl system, the former being in effect the first homologue of the latter.

Winstein^{50,51} proposed the non-classical ion (64) as the product-forming intermediate in the solvolysis of norbornyl derivatives to account for, among other phenomena, the marked difference in rate of reaction of the *exo* and *endo* derivatives. *Exo*-2-norbornyl brosylate (62, R=OBs) solvolyses about 350 times faster than the corresponding *endo* compound. Winstein attributes this to participation of the C-6 - C-1 sigma bond during ionisation of the *exo* isomer forming the non-classical ion

(64). Brown^{96,97}, however, has argued that the rate of solvolysis of exo-2-norbornyl brosylate, rather than being enhanced, is, in fact, normal; and that the rate of solvolysis of the endo-2-brosylate is reduced by steric hindrance in the transition state due to the proximity of the endo hydrogen atoms on C-5 and C-6 to the departing brosylate group. These two points of view have been the subject of considerable controversy⁹⁸.

Schleyer⁹⁹ has extended the observation by Foote¹⁰⁰, that rates of solvolysis of secondary derivatives are linearly correlated with the carbonyl stretching frequency of the corresponding ketone, into a general equation 1. which can be used to predict the rate of solvolysis of any secondary tosylate $\log k_{\text{rel.}} = 0.125(1715 - \nu_{\text{co}}) + 1.32 \sum (1 + \cos 3\phi) + (GS - Ts)/1.36$ where $k_{\text{rel.}}$ is the predicted rate relative to cyclohexyl tosylate at 25°C. The first term in the equation gives a measure of the internal bond angle strain, the second term a measure of the torsional strain where ϕ is the average smaller torsional angle around each of the C-C bonds adjacent to the leaving group, and the last term estimates

the difference in non-bonded interactions in going from ground state (GS) to transition state (TS).

Using this equation Schleyer⁹⁹ has found good agreement between predicted rates and observed rates for the solvolysis of tosylates which are not thought to involve anchimeric assistance, for example endo-2-norbornyl tosylate. The observed rates of some compounds e.g. exo-2-norbornyl tosylate are considerably faster than the predicted rate and Scheyer attributes the difference to anchimeric assistance.

The predicted rate of exo-6-bicyclo(3,2,1) octyl tosylate (93, R=OTs) relative to cyclohexyl tosylate (Table 8) was calculated using equation 1. The carbonyl frequency is that of bicyclo (3,2,1) octan-6-one and the torsional angles were estimated from models. The uncertainty as to the magnitude of one of the angles and the non-bonded interactions is reflected in the possible error of the calculated relative rate. This rate is similar to the observed rate which, however, does not take into account possibility of ion pair return.

Table 8.

Tosylate	Ketone Vco	ϕ	GS-TS	log rel.		log (achimeric assistance)
				Calc.	Obs.	
<u>endo-2-norbornyl</u>	1751	0,40	1.3	-0.2	+0.2	-
<u>exo-2-norbornyl</u>	1751	0,40	0.3	-0.6	2.71	3.3
<u>exo-6-bicyclo(3,2,1) octyl</u>	1743	0,30?	0.2 \pm 0.1	0.5 \pm 0.2	0.4	-

Nevertheless, any anchimeric assistance in this system is, at best, small in magnitude.

This result is somewhat surprising as (a) analysis of the products from the acetolysis of the exo-tosylate (93, R=Ac) produces compelling evidence in favour of the involvement of bridged intermediates; and (b) the geometrical requirements for assistance are satisfied as the C-1 - C-2 bond in the bicyclo-octyl skeleton is approximately trans- anti- parallel to the departing group.

There appear to be two possible explanations which could account for these anomalies. Firstly, if ionisation of the tosylate group of (93, R=OTs) is accompanied by delocalisation of the C-4 - C-5 bond then the bridged ion formed (107) must be similar in energy to the classical 6-cation (104). Alternatively, the rate determining step may involve simple ionisation of the molecule to the cation (104) which could then, in a subsequent step¹⁰¹, lead to the bridged intermediate.

The relative instability of the bridged ion (107) manifests itself in (1) the lack of substantial hydride shift in the bridged ion (108) to give (107) compared with

the facile shift in the opposite direction; (2) the reluctance of 3- Δ^3 cyclopentenyl propyl tosylate to give bicyclic products under acetolysis conditions (see section 4) and; (3) the absence of detectable anchimeric assistance to the solvolysis of the exo-6-tosylate (93, R=OTs). Moreover, the lack of anchimeric assistance in a compound similar to norbornyl tosylate in structure is surprising and would seem to suggest that such a phenomenon is not a prerequisite for the involvement of bridged ions in a reaction.

The difference in reactivity of exo-2-norbornyl tosylate and exo-6-bicyclo (3,2,1) octyl tosylate might derive from the fact that the C-6 - C-1 bond in the former is in a five-membered ring and perhaps relief of angle strain in this ring on the formation of a bridged intermediate contributes to the marked participation of that bond. The equivalent trans-anti-parallel bond (the C-4 - C-5 bond) in the latter case lies in a six-membered ring.

EXPERIMENTAL

Exo-bicyclo(3,2,1)octan-6-ol (93, R=OH).— A mixture of the epimeric bicyclo(3,2,1)octan-6-ols (25:1; g.l.c.) was prepared by the method of Wiberg and Hess⁷¹. Crystallisation from pentane afforded the predominating exo-isomer, m.p. 143-144.5° (lit.⁷¹ 144-145°); broadened d at 5.70 (1H-6; J = 7 c./sec.).

The exo-6-acetate (93, R=OAc) was prepared by reacting the alcohol (98 mg.) with acetic anhydride (3 ml.) in dry pyridine (3 ml.) and the crude product (120 mg.) purified by short-path distillation, $[n]_D^{22}$ 1.4682, ill-resolved q at τ 5.07 (1H-6; J = 7, 3 c./sec.) (Found: C, 71.1; H, 9.8. C₁₀H₁₆O₂ requires C, 71.4; H, 9.6%).

exo-bicyclo(3,2,1)octan-6-toluene-p-sulphonate (93, R=OTs).— Chilled solutions of exo-bicyclo(3,2,1)octan-6-ol (608 mg.) in dry pyridine (6 ml.) and toluene-p-sulphonyl chloride (1.225 g.) in the same solvent (5 ml.) were mixed and allowed to stand at room temperature overnight. The reaction mixture was poured onto ice,

extracted with ether and the solvent removed (traces of pyridine were expelled by azeotropeing with benzene). The residual yellow oil crystallised slowly from methanol yielding the exo-tosylate (1.17 g.) m.p. 51-52°; μ at τ 5.22 (1H-6; $J = 7, 3$ c./sec.). (Found: C, 64.1; H, 7.0. $C_{15}H_{20}O_3S$ requires C, 64.3; H, 7.2%).

Bicyclo(3,2,1)octan-6-one.- exo-Bicyclo(3,2,1)octan-6-ol (1.20 g.) in acetone (20 ml.) was treated with Jones reagent³² at 0° for 15 min. Normal work-up procedure furnished bicyclo(3,2,1)octan-6-one (1.02 g.) which was purified by vacuum sublimation (70°/13 mm.) m.p. 153.5-157° (lit.⁷¹ 155-157°); ν_{\max} . 1743 cm^{-1} .

endo-bicyclo(3,2,1)octan-6-ol (94, R=OH).- Bicyclo(3,2,1)octan-6-one (674 mg.) was heated with excess lithium aluminium hydride in refluxing diethyl ether. The product after vacuum sublimation (655 mg.) was found (g.l.c.) to be a mixture of the endo and exo alcohols (93:7). Crystallisation from pentane yielded pure endo-bicyclo(3,2,1)octan-6-ol (94, R=OH) m.p. 192-194°; ν_{\max} . 3622 cm^{-1} ; μ at τ 5.50 (1H-6; $W^{1/2} = 22$ c./sec.). (Found: C, 76.0; H, 11.1. $C_8H_{14}O$ requires C, 76.2; H, 11.2%).

The corresponding endo-6-acetate (94, R=OAc) was obtained in high yield by acetylation of the alcohol in pyridine and purified by short-path distillation in vacuo; $[n]_D^{23}$ 1.4672, m at γ 4.90 (1H-6; $W^{1/2} = 22$ c./sec.). (Found: C, 71.0; H, 9.4. $C_{10}H_{16}O_2$ requires C, 71.4; H, 9.6%).

endo-bicyclo(3,2,1)octan-6-toluene-p-sulphonate (94, R=OTs).- Endo-bicyclo(3,2,1)octan-6-ol (157 mg.) and toluene-p-sulphonyl chloride were reacted in the manner described for the exo isomer. The crude product crystallised from pentane giving the endo-tosylate (13, R=OTs) (268 mg.), m.p. 43.5-44.5°; m at γ 5.08 (1H-6; $W^{1/2} = 23$ c./sec.). (Found: C, 64.3; H, 7.3. $C_{15}H_{20}O_3S$ requires C, 64.3; H, 7.2%).

Bicyclo(3,2,1)oct-6-ene (96).- exo-bicyclo(3,2,1)octan-6-toluene-p-sulphonate (94, R=OTs), (500 mg.), was heated in refluxing dry collidine (12 ml.) for 30 min. On cooling, water was added, and the reaction mixture extracted several times with pentane. The combined extracts were washed successively with dilute H.C.L. saturated $NaHCO_3$ solution, and then with water. The crude product obtained by drying of the solution and evaporation of the solvent in vacuo at 0° was allowed to sublime at -5° (760 mm.) giving bicyclo(3,2,1)oct-6-ene (96),

(125 mg.), m.p. 111-112° (lit.⁸⁷ 106-108°); n.m.r. signals at τ 4.15 (sharp singlet; 1H-6, 1H-7) and 7.43 (broad singlet; 1H-1, 1H-5). (Found: m/e 108.09389. C_8H_{12} requires m/e 108.09390.)

2-(1-pyrrolidinyl)bicyclo(3,2,1)octane.- A solution of acrolein (10 g.) in dioxan (40 ml.) was added over a period of 1 hr. to a stirred solution of 1-(1-pyrrolidinyl)-cyclopentene⁹² (20 g.) in dry dioxan (40 ml.) at 0°. After a further 3 hrs., during which the mixture had attained room temperature, the solvent was removed in vacuo and the residual oil fractionated to give 2-(1-pyrrolidinyl)-bicyclo(3,2,1)octan-8-one (12.7 g.) b.p. 120-121°/0.1 mm. This ketoamine (12.0 g.) and hydrazine hydrate (18 ml.) were added to a solution of sodium (5.0 g.) in diethylene glycol (140 ml.). After heating at 140° for 1 hr., water and excess hydrazine hydrate were removed by distillation, and the temperature was then maintained at 210° for a further 5 hrs. The cooled reaction mixture was diluted with water (450 ml.) and extracted with ether. After removal of the solvent, fractionation of the crude product furnished 2-(1-pyrrolidinyl)-bicyclo(3,2,1)octane (7.23 g.) b.p. 86-88°/0.1 mm.

Bicyclo(3,2,1)oct-2-ene (97).- 2-(1-pyrrolidinyl)-bicyclo(3,2,1)octane (4.0 g.) and hydrogen peroxide (100 vols.; 12 ml.) were heated in refluxing methanol (50 ml.) for 4 hr. The excess peroxide was destroyed by the addition of a few milligrammes of 10% palladium on charcoal catalyst. Removal of the catalyst and then evaporation of solvent in vacuo gave the corresponding amine oxide which on pyrolysis (160°/0.1 mm.) yielded oily bicyclo(3,2,1)oct-2-ene (0.52 g.). Filtration of this oil in pentane through neutral alumina (Woelm: Grade I) and then sublimation at -5° (760 mm.) gave colourless plates m.p. 42-44° (sealed capillary: lit.⁸⁸ 43-45°).

Bicyclo(3,2,1)octan-2-one.- A solution of 2-(1-pyrrolidinyl)bicyclo(3,2,1)octane (1.50 g.) and mercuric acetate (10.5 g.) in 5% aqueous acetic acid was stirred at 100° for 2½ hr. The yellow crystalline precipitate was filtered off, washed with 5% aqueous acetic acid, then with acetone, and the combined filtrates evaporated to dryness under reduced pressure. Water (50 ml.) was added and hydrogen sulphide passed through the turbid solution until precipitation was complete. The mixture was filtered, the filtrate saturated with potassium carbonate and the product extracted into ether. Sublimation (80°/16 mm.) of the crude

product obtained by removal of the solvent afforded bicyclo(3,2,1)octan-2-one (530 mg.) m.p. 124-127° (lit.⁹¹ 127-129°).

exo- and endo-bicyclo(3,2,1)octan-2-ols (100 and 102, R=OH).- Reaction of bicyclo(3,2,1)octan-2-one (400 mg.) with excess lithium aluminium hydride in refluxing diethyl ether⁹¹ afforded a mixture (381 mg.) which was shown by g.l.c. to comprise exo-bicyclo(3,2,1)octan-2-ol (100, R=OH) (30%), and the corresponding endo isomer (102, R=OH) (70%).

A sample of this mixture (102 mg.) was acetylated in the manner described previously⁹¹. The product, after short-path distillation (91 mg.), was submitted to quantitative analysis by n.m.r. and shown to consist of the exo and endo-2-acetates in a ratio 3:7 (integration of $\text{CH}_3\text{.COO}$ -signals).

Bicyclo(2,2,2)oct-5-en-2-ol.- Diels-Alder reaction of vinyl acetate (32 g.) and cyclohexa-1,3-diene (15 g.) using the procedure described by Goering and Sloan⁷⁵ furnished 2-acetoxycyclo(2,2,2)oct-5-ene. Reaction of the crude acetate with lithium aluminium hydride led to bicyclo(2,2,2)oct-5-en-2-ol (7.4 g.) which after crystallisation from light petroleum had m.p. 166-168° (6.2 g.) lit.⁷⁵ 167.5-.69°).

Bicyclo(2,2,2)octan-2-ol (101 R=OH).- Bicyclo(2,2,2)-oct-5-en-2-ol (500 mg.) was hydrogenated over 10% Pd-C (50 mg.) in ethyl acetate (20 ml.); hydrogen uptake was 1 mol. equivalent. Recrystallisation of the product from pentane yielded bicyclo(2,2,2)octan-2-ol (436 mg.) m.p. 221.5-223° (lit.⁷⁴ 221-222°).

The corresponding acetate⁹¹ was prepared in the usual manner.

Bicyclo(2,2,2)oct-2-ene (98).- Bicyclo(2,2,2)oct-5-en-2-ol (840 mg.) was oxidised with Jones Reagent³² at 0°. After work-up the crude product was converted into the semicarbazone which crystallised from benzene as colourless needles (440 mg.) m.p. 176-178°. (Found: C, 60.2; H, 7.3; N, 23.5. C₉H₁₃ON₃ requires C, 60.3; H, 7.3; N, 23.5%).

The semicarbazone (406 mg.) in diethylene glycol (4 ml.) was heated at 100° until a homogeneous solution was attained. Potassium hydroxide pellets (400 mg.) were added and the temperature was raised to 190° for 3½ hr. The crude olefin, which had completely sublimed into the reflux condenser, was recovered with pentane and then the solvent removed in vacuo at 0°. Sublimation of the residue

(40°/760 mm.) furnished bicyclo(2,2,2)oct-2-en (173 mg.) m.p. 114-116° (lit.⁸⁹ 111-112°).

exo- and endo-bicyclo(3,2,1)octan-3-ols.- Bicyclo-(3,2,1)octan-3-one⁹³ (216 mg.) and lithium aluminium hydride (100 mg.) were reacted in refluxing diethyl ether. A mixture of the spimeric bicyclo(3,2,1)octan-3-ol (189 mg.) in a ratio of 3:1 (g.l.c.) was obtained and separated by preparative-scale t.l.c. (chloroform as solvent).

The predominating isomer, exo-bicyclo(3,2,1)octan-3-ol crystallised from pentane and had m.p. 101-102° lit.⁹³ 101.5-102°). The endo isomer m.p. 203-204°(lit.⁹³ 206-206.5°) also crystallised from pentane. Confirmation of structure assignments was obtained by n.m.r.⁹⁴ .

The corresponding acetates were prepared by the standard procedure, exo-3-acetate. (Found: C, 71.2; H, 9.6. C₁₀H₁₆O₂ requires C, 71.4; H, 9.6%) endo-3-acetate (Found: C, 71.1; H, 9.5. C₁₀H₁₆O₂ requires C, 71.4; H, 9.6%).

Tricyclo(3,2,1,0^{2,7})octane (99).- Tricyclo(3,2,1,0^{2,7})-octan-6-one⁹⁵ (1.5 g.) was heated with a solution of semicarbazide hydrochloride (2.25 g.) and hydrated sodium acetate (3.6 g.,) in water (9 ml.) at 40° for 12 hr. The crude product was filtered off, and crystallised from aqueous ethanol to give the semicarbazone (1.52 g.).

Wolff-Kishner reduction of this derivative using the procedure described for the preparation of bicyclo(2,2,2)oct-2-ene gave tricyclo(3,2,1,0^{2,7})octane (422 mg.), which sublimed (-5°/760 mm.) as colourless needles m.p. 87-89° (lit.⁹⁰ 91-92°).

Buffered Acetolyses.- In a typical experiment exo-bicyclo(3,2,1)-octan-6-toluene-p-sulphonate (93, R=OTs) (93 mg.) was heated in acetic acid (5 ml.) containing sodium acetate (30 mg.) at 110° in a sealed ampoule for 18 hr. The reaction mixture was cooled, diluted with water and extracted with pentane. The pentane extract was washed with aqueous sodium carbonate, dried and the solvent removed. The products were separated by chromatography over silica gel into hydrocarbon (35-40% yield) and acetate (60-65% yield) fractions.

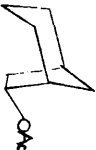

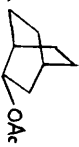




Un-buffered acetolyses.- In a typical reaction bicyclo(2,2,2)-oct-2-ene (98) (20 mg.) was treated with acetic acid (2 ml.) containing toluene-p-sulphonic acid (2 mg.) at 110°C in a sealed ampoule for 24 hr. The above work-up furnished high yields (80-90%) of acetate products. (Since aliquot sampling showed that the proportion of the products from bicyclo(3,2,1)oct-6-ene was still changing

fairly rapidly even after a reaction time of 24 hr. the reaction was allowed to continue in this case for 1 week).

Rate measurements.- In a typical experiment the tosylate (93, R=OTs)(58 mg.) was dissolved in acetic acid at room temperature containing anhydrous sodium acetate (21 mg.) and the mixture shaken to ensure homogeneity. 3 ml. portions were sealed into ampoules which were then heated at 80° (or 100°) in a thermostat, for various time intervals. The optical density of the various aliquots was measured at 261 m μ in the ultraviolet. An infinity reading allowed an estimation of the percentage unreacted tosylate in each case and a graph of the log. of this against time gave a value for the rate constant of the reaction. This procedure was repeated about 4 times for each tosylate at any one temperature and the results were highly reproducible varying only about 5%. The accuracy of the method was checked by solvolysing cyclohexyl tosylate for which a rate constant within 2% of the correct value was obtained.

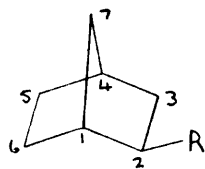
Table 6.

Chemical shifts of the CH_3CO_2 - resonances in the
bicyclo(3,2,1)- and bicyclo(2,2,2)-acetates

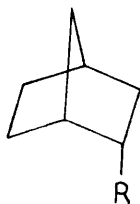
Compound							
$\text{CH}_3\text{COO-}$ Chemical Shift (a)	199.5	206.3	203.3	204.7	200.7	198.7	202.1

(a)

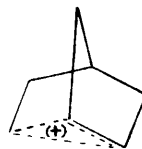
in c./sec. from internal T.M.S. at 100 Mc./sec.



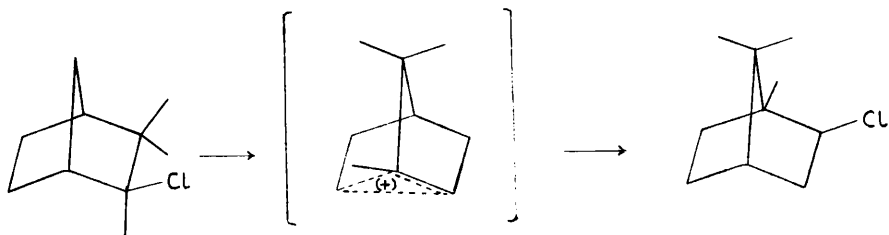
62



63



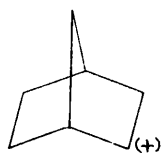
64



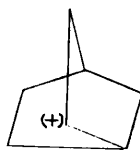
65

67

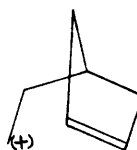
66



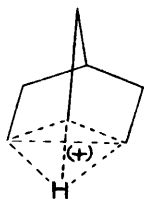
68



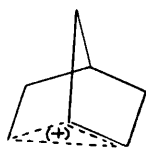
69



70



71



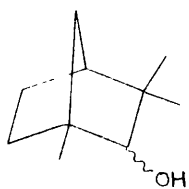
64



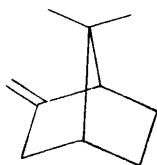
64a



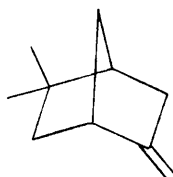
64b



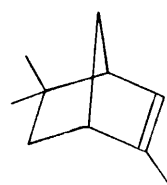
72



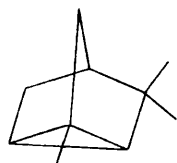
73



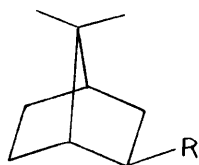
74



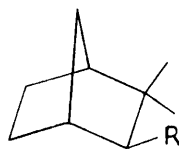
75



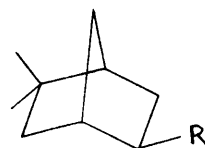
76



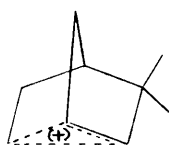
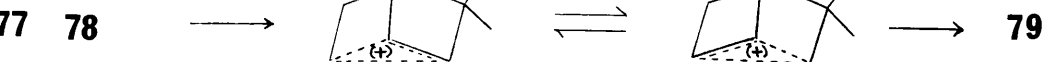
77



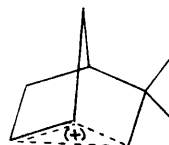
78



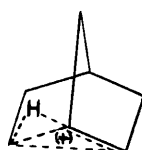
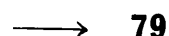
79



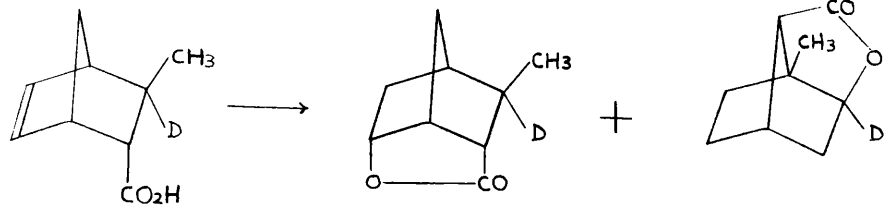
80



81



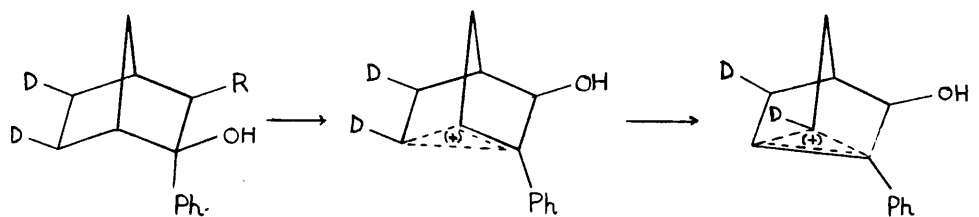
82



83

84

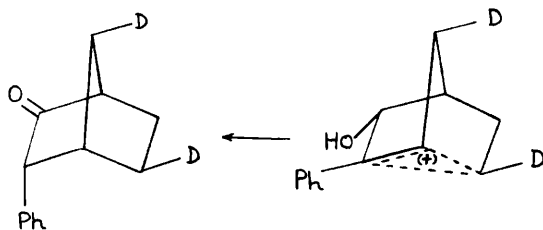
85



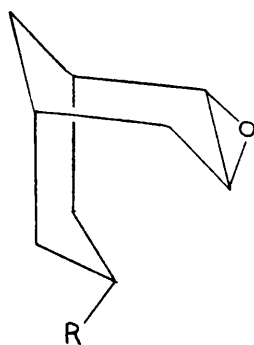
86

87

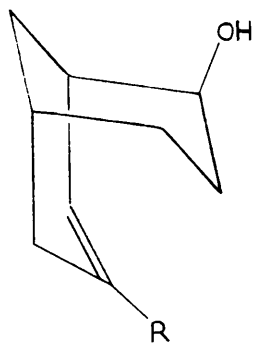
88



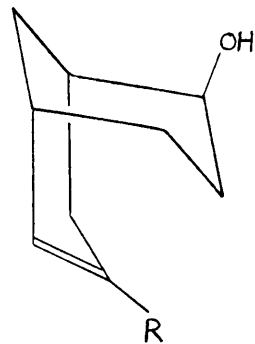
89



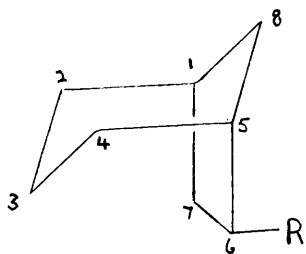
90



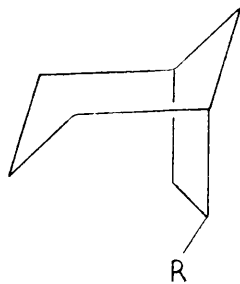
91



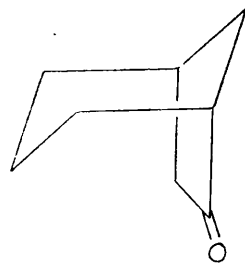
92



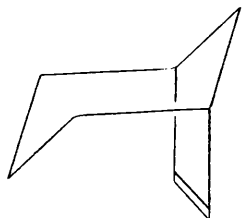
93



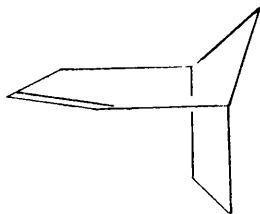
94



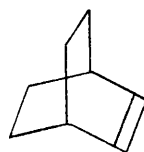
95



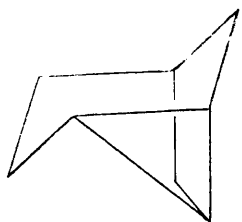
96



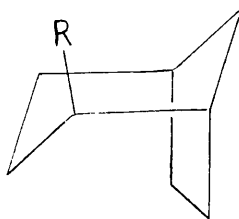
97



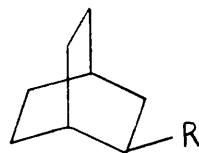
98



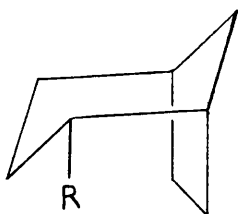
99



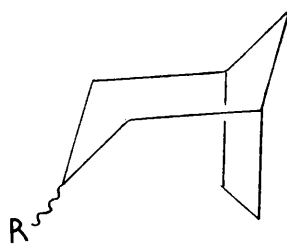
100



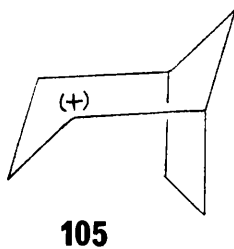
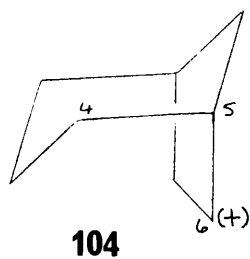
101



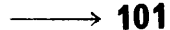
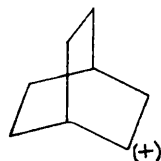
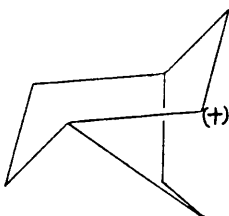
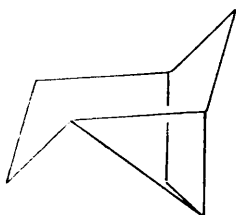
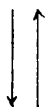
102



103



100



101

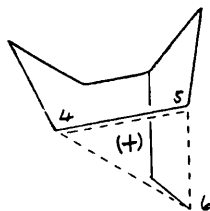
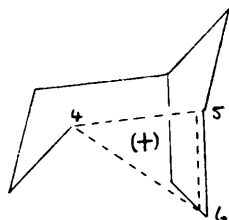
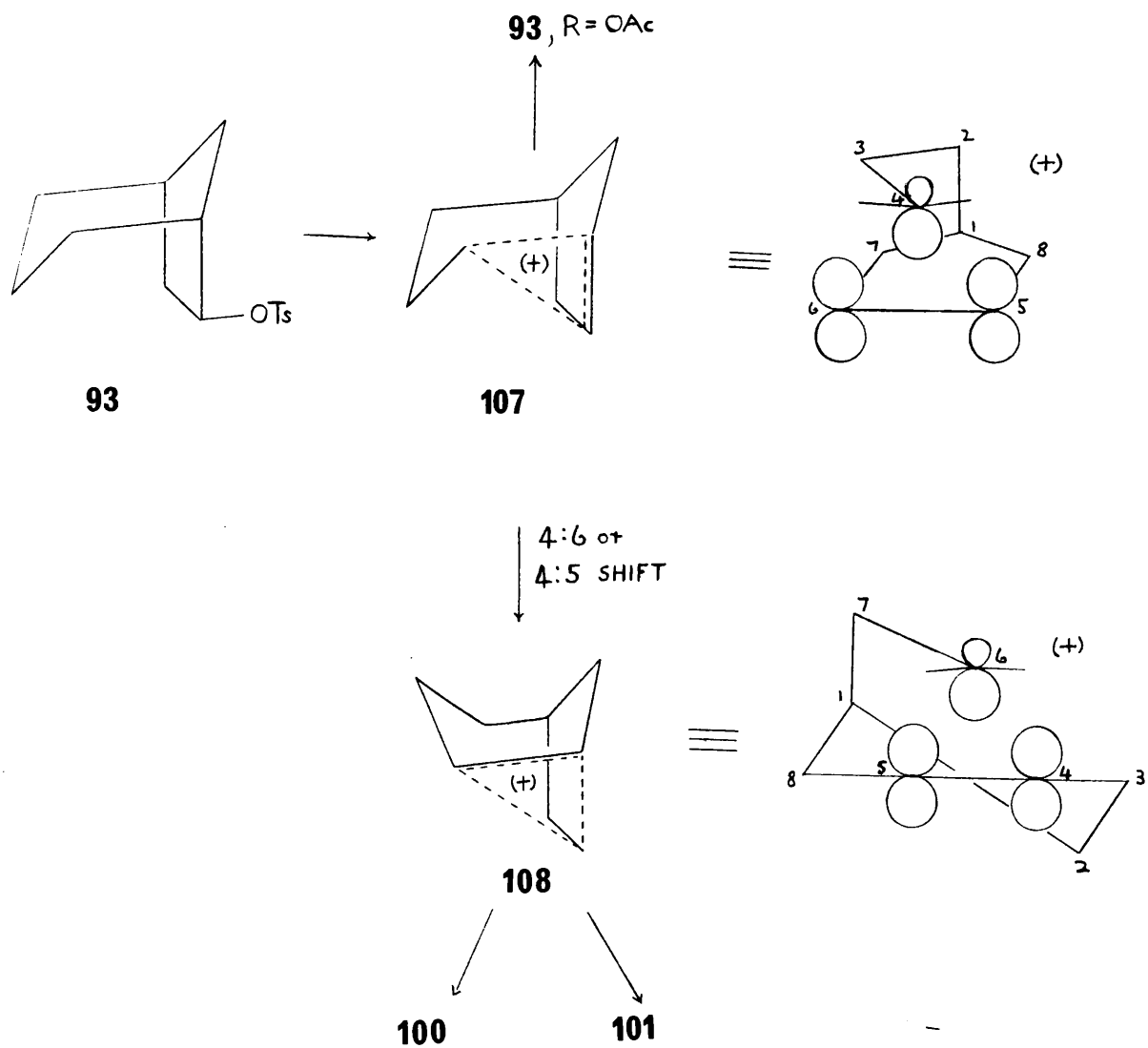
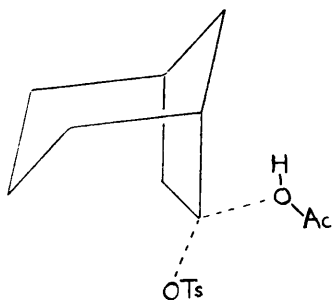
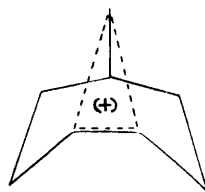


Figure 1.

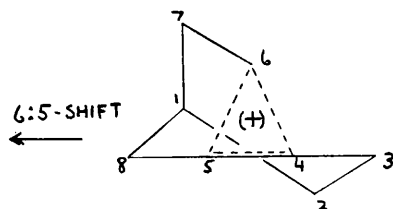
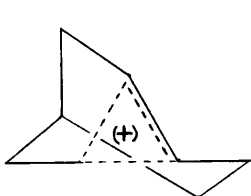




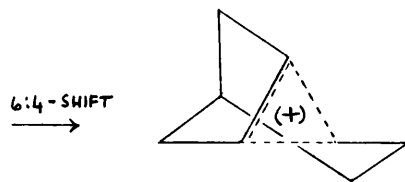
109



110



108



107

' π -Routes' to bicyclic systems

It is well established that an olefinic double bond can assist the solvolytic displacement of a halide or sulphonate ion. In the case of the allylic system the effect of conjugation of the reacting centre with the double bond or benzene ring is pronounced. The rate enhancement is attributed to stabilization of the transition state, the positive charge of the intermediary¹⁰² carbonium ion being delocalised by π -bond overlap. This effect is not unique to the allylic system and occurs whenever the p-orbitals of the double bond are in a favourable position for overlap with the vacant p-orbital of the carbonium ion. This is evident in the solvolyses of various homoallylic systems, for example cholesteryl tosylate¹⁰² and 7-norbornenyl derivatives^{103,104}. This type of ion, where delocalisation of the positive charge is possible, is generally termed a 'non-classical' ion. This term is not normally used

in the case of allylic and benzylic cations where the molecular orbitals are formed purely by π -overlap between atomic orbitals as in (111). In the case of 'non-classical' ions analogous molecular orbitals can only be formed by at least partial σ -overlap between atomic orbitals. This may be small as in the case of the cholesteryl cation (112) where overlap between the p-orbitals on C-5 and C-6 is π , and the overlap between the p-orbitals on C-3 and C-5 is partially π and partially σ ¹⁰⁵. In the case of the 7-norbornenyl cation¹⁰⁴ (113) however, the bonding has been treated as pure p- π overlap between C-2 and C-3 and pure p- σ overlap between C-7 and C-2 and C-7 and C-3.

As well as producing rate enhancement, double bond participation during solvolysis can manifest itself in the type of product isolated. Whereas exo-7-norbornenyl bromide (114)¹⁰⁴ solvolyses to an unrearranged product, anti-bicyclo (2,2,2)oct-5-en-2-yl tosylate¹⁰⁶ gives the tricyclic compound (115) as the major product. Although both reactions proceed faster than the corresponding saturated compounds no tricyclic

product is produced in the former case because of the angle strain involved in its formation.

Winstein^{50,51} has written the carbonium ion formed from the solvolysis of 2-norbornyl derivatives as (116). This represents from the valence bond notation the contribution of three canonical forms (116a) 116b, 116c) to the mesomeric cation. Entrance into the ion (116) should be possible via any of these three ions. Solvolysis of 2-norbornyl derivatives would produce either ion (116a) or (116b) and solvolysis of 2-(Δ^3 -cyclopentenyl) ethyl derivatives ion (116c). Both Lawton¹⁰⁷ and Bartlet and Bank¹⁰⁸ have investigated compounds of the latter type and found that the reaction gives exclusively exo-2-norbornyl derivatives with rate enhancement, suggesting that the double bond participates with the developing ionisation the primary function to give the 'non-classical' ion (116). Winstein⁷⁶ has proposed the general term ' Π -route' to distinguish the formation of a bridged ion from compound (117) by participation of the

π -electrons of the double bond, from the σ -route, in which the three centre, electron-deficient bond of (116) is formed σ -delocalisation from starting materials (118). That the π -route to the 'non-classical' ion is feasible is reflected in the suggestion of Dewar¹⁰⁹ who regards the bonding in the ion as consisting of a dative bond between a pair of π -electrons and a bridging atom tetrahedral in nature. He maintained that only π -electrons are capable of such dative bonding since σ -electrons are sterically inhibited from such participation.

The possible orbital structure of the non-classical bridged 2-norbornyl cation is shown (119)¹¹⁰.

In this representation there is considerable σ -bonding between an sp^3 orbital of C-6 and the two p-orbitals of C-1 and C-2.

Double bond 'capture' of carbonium ions has been used as a means of entry into several other non-classical ions. LeNy⁸⁴ found that Δ^4 -cycloheptenyl methyl tosylate underwent acetolysis with rate enhancement to give endo-bicyclo (3,2,1) octan-2-yl acetate (120, R=OAc). This is consistent with the

intervention of the bridged ion (121) which has been proposed as an intermediate in the acetolysis of the bicyclic tosylate (120, R=OTS)⁷⁵. The ion (122) has been approached by two σ -routes by solvolyses of bicyclo (2,2,2) octan-2-yl (123, R=OTS)^{74, 75} and exo-bicyclo (3,2,1) octan-2-yl tosylates (124, R=OTS) and Winstein has investigated a π -route to this ion by acetolysis of Δ^3 -cyclohexenylethyl brosylate.⁷⁶ The bicyclic products (80%) are identical in composition to those obtained from (123 and 124, R=OTS).

The bicyclo (3,3,1) nonyl system has also been entered by way of a π -route. Several groups of workers have found that solvolysis of Δ^4 -cyclooctenyl carbonyl derivatives give endo-2-bicyclo (3,3,1) nonyl products.^{111, 112, 113, 114} By comparison with Le Ny's study in the bicyclo octyl system this might suggest that the non classical ion (126) is the intermediate as this accounts for the stereospecificity in product formation. However the acetolysis of endo-2-bicyclo (3,3,1) nonyl brosylate yields a mixture of exo and endo acetates

which appears to exclude the bridged ion (126) as an important intermediate in the acetolysis of (127, R=OTs) and casts some doubt upon its role in the acetolysis of (125, R=OBs). The major product forming intermediate in both these reactions is thought to be the classical ion (128) which, when formed from the unsaturated brosylate (125, R=OBs) is not protected on the endo side by the departing anion and this may then account for the exclusive formation of endo product from that compound.

A further example of a π -route to a bicyclic compound is 3-(Δ^2 cyclohexenyl) propyl tosylate which has been shown¹¹⁵ to cyclise on acetolysis to give as well as the bicyclo (4,3,0) nonyl acetate (129), the bridged bicyclic acetate (130).

π -Route to the 6-bicyclo (3,2,1) octyl cation

Since we have postulated the ion (107) as the intermediate species in the rearrangement of *exo*-bicyclo (3,2,1) octan-6-yl tosylate (93, R=OTs) we decided to investigate a possible π -route to this ion. It was hoped to realise this by solvolysis of 3-(Δ^3 -cyclopentenyl) propyl derivatives (131).

If ion (107) is indeed the intermediate the bicyclic products from (131) should be identical in nature and composition to those obtained from the acetolysis of *exo*-bicyclo (3,2,1) octan-6-yl tosylate.

Acetolysis of 3-(Δ^3 -cyclopentenyl) propyl *p*-nitrobenzene sulphonate had been shown¹¹⁶ to yield no bicyclic acetates but in view of recent work¹¹⁷ on the buffering of acetolysis reactions it was hoped to obtain more useful results.

When an alkyl arenesulphonate is solvolysed in a non-basic solvent a strong sulphonic acid is produced.

Unstable products can be protected by addition of a sufficiently strong base to convert the sulphonic acid to an inert sulphonate salt. The most commonly used base is sodium or potassium acetate, which being good nucleophiles can however affect the product composition through direct displacement. This is evident in the acetolysis of 5-hexenyl p-nitro-benzenesulphonate which from rate calculations would be expected to yield 37% of cyclic product via double bond participation. Using acetate as a buffer only 18% of cyclic products were obtained¹¹⁷. However, using urea as a buffer this figure rises to 36-38% as the concurrent SN2 reaction by acetate ion is eliminated.

Δ^3 -cyclopentenyl tosylate¹⁰⁷ was prepared via hydroboration of cyclopentadiene and alkylated with diethyl malonate. Hydrolysis and decarboxylation afforded the acid (132, X=CO₂H) which was converted into the diazoketone and then by treatment with silver oxide in methanol into the homologous methyl

ester (133). Reduction of the methyl ester with lithium aluminium hydride and reaction of the resultant alcohol with tosyl chloride in pyridine afforded the liquid tosylate (131 ,X=OTS) which although labile could be stored for a short time in cold ether.

Acetolysis of the tosylate using sodium acetate as a buffer gave a high yield of the corresponding primary acetate (131,X=OAc) with no trace of bicyclic products. The reaction was repeated using urea as the buffer in a hope that any participation of the double bond would become evident in this medium. Unfortunately the sole acetate product was again (131 ,X=OAc).

The lack of detectable amounts of bicyclic products from (131 ,X=OTS) is somewhat surprising when compared to the exclusive formation of bicyclic products from 2-(Δ^3 -cyclopentenyl) derivatives. The cation from the former might be expected to cyclise

with the introduction of less angle strain. The extra degrees of freedom involved by the lengthening of the chain cannot solely account for the absence of bicyclic products as 3-(Δ^2 -cyclohexenyl) propyl derivatives, yield bridged bicyclic products on acetolysis. This would appear to be another manifestation of the difference in relative stabilities of the norbornyl cation (116) and the 6-bicyclo octyl cation (107) discussed at some length in the previous section.

Experimental

Δ^3 -cyclopentenol - Diborane, generated by the addition of sodium borohydride (1.9 g) in diglyme (50 ml.) to boron trifluoride etherate (10 g.) in the same solvent (20 ml.), was passed into a solution of freshly distilled cyclopentadiene (20 g.) in anhydrous ether (80 ml.) at 0°C over a period of 30 min., while a slow stream of nitrogen was maintained. After a further 30 min. at 20°, the excess cyclopentadiene and solvent were removed under vacuum.

The residual oil was treated in ether with 3M sodium hydroxide followed by the slow addition of 30% hydrogen peroxide. The organic layer was separated and the aqueous solution extracted with ether. The ether washings were combined, dried and the solvent was removed to yield crude Δ^3 -cyclopentenol¹¹⁸. This was then distilled and the fraction in the range 60-70° (36 mm.) collected: i.r. ν_{max} . 3600, 3080, 1640, 1040, 840, 680 cm^{-1} .

Δ^3 -cyclopentenyl tosylate¹¹⁸ - Chilled solutions of Δ^3 -cyclopentenol (5 g.) in dry pyridine (20 ml.) and toluene-p-sulphonyl chloride (15 g.) in the same solvent (25 ml.) were combined and allowed to stand overnight at room temperature. Workup furnished a crude product which on crystallisation from light petroleum yielded pure Δ^3 -cyclopentenyl tosylate (10.5 g.) m.p. 52.5 - 54° (lit.¹¹⁸ m.p. 53.4 - 54.2°); n.m.r., q at τ 2.40 (4H-aromatic H's); s at τ 7.57 (3H-aromatic methyl).

Δ^3 -cyclopentenyl malonic acid.- Sodium hydride (1.05 g.) was added gradually to diethyl malonate (8 g.) in xylene (40 ml.). Once effervescence had ceased Δ^3 -cyclopentenyl tosylate (10 g.) in xylene was added and the mixture heated in an oil bath at approximately 120°C a heavy white precipitate of sodium tosylate was formed. The reaction mixture was then filtered and the solvent removed by distillation under reduced pressure. The crude product (9.5 g.) was hydrolysed with 50% aqueous

ethanolic potassium hydroxide (50 ml.) under reflux for 2 hr. Extraction of the product into ether followed by removal of the solvent afforded Δ^3 -cyclopentenyl malonic acid (6.6 g.) m.p. 144-148°, (lit.¹⁰⁷ m.p.. 149-150°).

Δ^3 -cyclopentenyl acetic acid - Δ^3 -cyclopentenyl malonic acid (6.5 g.) was heated in refluxing dry pyridine for 4 hours. The reaction mixture was then cooled, poured into water and extracted with ether. The ether extracts were combined, dried and the solvent removed under vacuum to give Δ^3 -cyclopentenyl acetic acid (4.6 g.) which was used in the next stage without further purification.

Methyl 3-(Δ^3 -cyclopentenyl) propionate - Δ^3 -cyclopentenyl acetic acid (4.5 g.) was converted into its chloride by treatment with excess oxalyl chloride in refluxing benzene. The solvent was removed and the product purified for the next stage by distillation under reduced pressure, the fraction (4.3 g.) between 150-160° (2 mm.) being collected.

The acid chloride (4.3) in ether (15 ml.) was added with stirring to a three molar excess of diazomethane¹¹⁹ in the same solvent at 0°C. The mixture was allowed to stand for 6 hours at room temperature and the solvent and excess reagent removed under vacuum affording the diazoketone (4.5 g.).

Small portions of silver oxide were added over a period of an hour¹¹⁹ to a stirred solution of the diazoketone (4.5 g.) in methanol at 60°. The reaction was stirred until the evolution of nitrogen ceased and then filtered. Removal of the solvent under vacuum furnished methyl 3-(Δ^3 -cyclopentenyl) propionate (3.6 g.), which was used in the next stage without further purification.

3-(Δ^3 -cyclopentenyl) propanol - The crude methyl ester (3.6 g.) was treated with lithium aluminium hydride (0.4 g.) in refluxing diethyl ether for saturated aqueous sodium sulphate was then added followed by

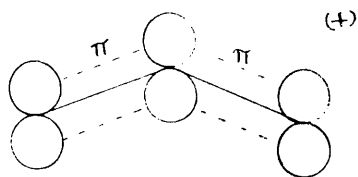
anhydrous sodium sulphate. Filtration and removal of solvent furnished a crude product which was distilled to yield 3-(Δ^3 -cyclopentenyl) propanol (2.1 g.), b.p. 108-110° (20 mm.) [lit.¹¹⁶ b.p. 112-112.5° (26 mm.)]; i.r., ν_{\max} . 3600, 3070, 1630, 685 cm^{-1} .

Reaction of the alcohol (0.5 g.) with excess acetic anhydride in pyridine afforded the acetate (0.51 g.), b.p. 115-117° (20 mm.) (lit.¹¹⁶ b.p. 113-115° (20 mm.)). The alcohol (0.8 g.) was reacted with toluene-p-sulphonyl chloride (1.6 g.) in pyridine (8 ml.). Workup gave 3-(Δ^3 -cyclopentenyl) propyl tosylate (1.3 g.) as an unstable oil which could be stored for a short time in chilled ether: n.m.r., τ at τ 2.41 (4H-aromatic H's); τ at τ 7.58 (3H-aromatic methyl).

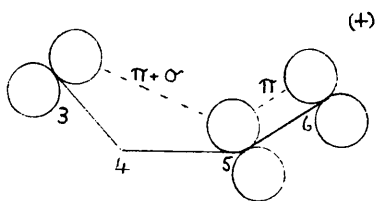
Solvolysis of 3-(Δ^3 -cyclopentenyl) propyl tosylate - The tosylate (0.2 g.) was treated with acetic acid (15 ml.) containing sodium acetate (0.05 g.) in a sealed tube at 110°C for 24 hr. The reaction was cooled, poured

onto water and extracted with pentane. The pentane extracts were combined, washed with saturated bicarbonate solution, dried and the pentane removed under vacuum at 0°C. The residue (0.11 g.) was shown (g.l.c.) to be essentially pure 3-(Δ^3 -cyclopentenyl) propyl acetate.

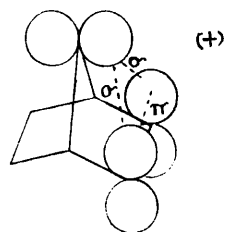
The above procedure was repeated substituting urea for sodium acetate as the buffer. The sole product from this reaction was again the unrearranged acetate.



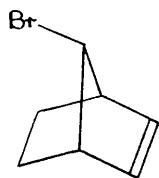
111



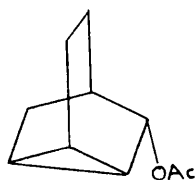
112



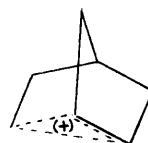
113



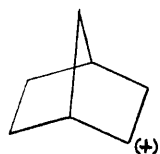
114



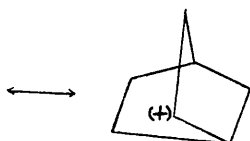
115



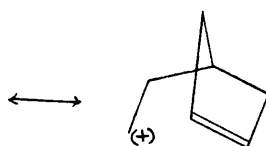
116



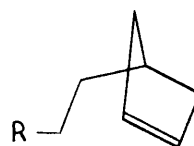
116a



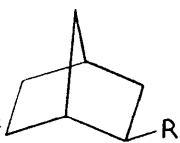
116b



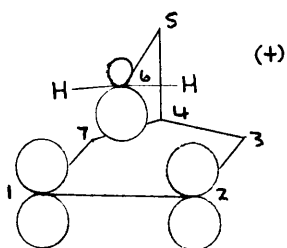
116c



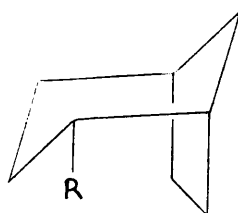
117



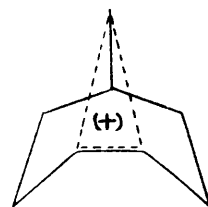
118



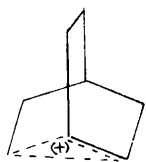
119



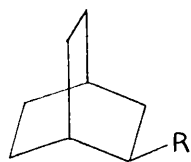
120



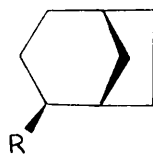
121



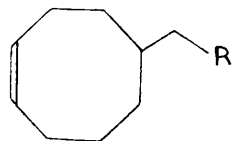
122



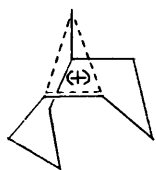
123



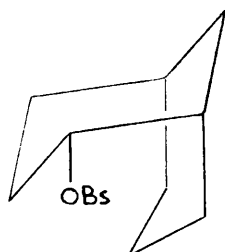
124



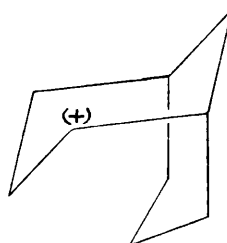
125



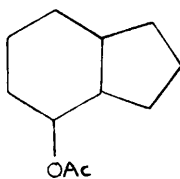
126



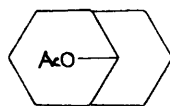
127



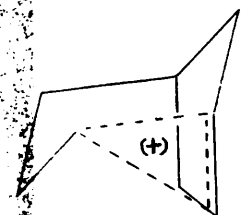
128



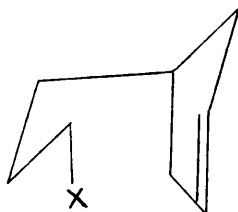
129



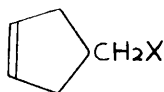
130



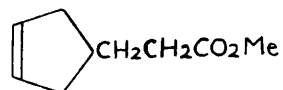
107



131



132



133

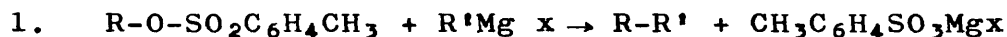
INTRODUCTION

Lithium aluminium hydride is a useful reagent for the reduction of various polar functional groups. The reaction procedure is similar to that followed in reactions involving Grignard reagents which the hydride closely resembles in its general pattern of behaviour. The fact that only polar groups are affected would suggest the intervention of a polar mechanism although it is unlikely that direct attack by hydride ion takes place as this does not account for the difference of reducing properties of various complex hydrides. Lithium aluminium hydride exists in ether solution as ion aggregates of strongly solvated lithium ions and aluminohydride ions $\text{AlH}_4^{(-)}$.

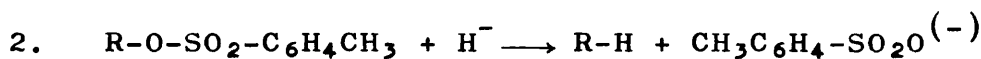
The most plausible mechanism would appear to be one in which hydrogen is transferred as hydride in a bimolecular nucleophilic displacement.¹²⁰ This suggestion has been supported by the observation that the configuration is inverted in the reduction of epoxides.¹²⁰

The reduction of an optically active secondary alkyl halide by lithium aluminium deuteride leads to an optically active hydrocarbon. For example the reduction of resolved phenethyl chloride by this reagent yields optically active α -deuterioethylbenzene¹²¹ and (1)-menthyl tosylate gives optically active 3-deuterio menthane.¹²² These results reinforce the conclusion that the reaction is a nucleophilic displacement (S_N2) type, the reduction of a resolved compound proceeding with Walden inversion to an active product.

A convenient conversion of an alcohol into the corresponding hydrocarbon can be achieved by reduction of the derived toluene-p-sulphonyl ester with lithium aluminium hydride. This process was developed as a logical extension¹²³ of the observation by Gilman¹²⁴ that Grignard reagents will react with esters of this type with the production of hydrocarbons according to the scheme 1.



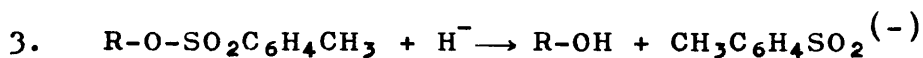
In a number of cases lithium aluminium hydride follows an analagous course as shown in scheme 2.^{125,126}



Hydride reduction by this path has been observed with primary and secondary^{122,127,128} alkyl tosylates. Esters of primary alcohols are reduced very rapidly, while esters of secondary alcohols are reduced more slowly and generally require heating for several hours.

This would be expected if the mechanism is indeed a nucleophilic displacement falling into line with the well known heterolytic decomposition of tosylates by nucleophilic reagents.¹²⁹

In other cases the reaction takes a different course and gives the parent alcohol according to scheme 3.



This mode of reduction will occur if there is steric hindrance to the normal path of the reaction.

Examples of this type of fission are found in the terpenoid field, for example, in steroidal 12- β -tosylates¹³⁰ and in the derivative of moradiol.¹³¹ The behaviour of various cholestanyl tosylates illustrates the influence of the steric factor in determining the proportion of hydrocarbon to alcohol formed on L.A.H. reduction. (see Table 9.)

Table 9.

Cholestanyl tosylate	Cholestanol formed (%)	Cholestane formed, (%)
3 β - ¹³²	17	83
6 α - ¹³³	57	38
7 β - ¹³⁴	-	92

Occasionally elimination may occur as an alternative to reduction of the ester and this process has been studied by Cram^{135,136} who has shown that the elimination is predominantly trans and bimolecular in nature.

Rearrangements during lithium aluminium hydride reductions of some alkyl halides and tosylates have been recorded. Thus, the reaction of lithium aluminium hydride with 3-bromo derivatives of cyclopentene, cyclohexene and cycloheptene proceeds as an allylic rearrangement by attack of hydride ion on C-1 of the ring as well as by simple nucleophilic

substitution of the bromide with hydride.¹³⁷ Such an allylic attack is indicated by the reaction of lithium aluminium hydride with the dibromo compound (134) which gives, among other products, the mono-bromo compound (135). Another example of this type of rearrangement is the hydride reduction of 3-chloro-1-butene¹³⁸ which yields cis-2-butene (5%), butadiene (8%), trans-2-butene (18%) and 1-butene (69%).

Examples of homoallylic rearrangements of toluene p-sulphonates have been noted. The reduction of cholesteryl tosylate yields isocholestene (136)¹²³ as a minor product and 7-substituted norbornadienes^{139,140,141} have been found to react with hydrides to afford norbornadiene (138) and the tricyclic hydrocarbon (139).

Winstein¹⁴² has demonstrated that 7-chloronorbornadiene (137, X=Cl) solvolyzes about 10^{14} _{times} faster than the corresponding saturated compound, suggesting that the double bonds greatly facilitate ionisation probably by the formation of a stable non-classical ion.

The formation of tricyclic hydrocarbon (139, Y=H) by hydride reduction of the 7-chloronorbornadiene constitutes chemical evidence of the interaction of a double bond and a developing carbonium ion at C-7.

The stereospecificity of the reduction has been established by reduction of (137, X=Cl) with lithium aluminium deuteride which leads exclusively to the endo deuterio compound (139, Y=D). A intermediate (140) has been postulated^{139, 141}, hydride attack (140, arrows) at position 2 yielding (139, Y=H) and at position 7 yielding (138, Y=H). The fact that no tricyclic products have been isolated from solvolyses of (137) is not surprising as the strain involved in the tricyclic molecule would shift the equilibrium quite far in the direction of the bicyclic structure. A hydride reduction is, however, irreversible and a reaction at any carbon other than C.7. of the intermediate (140) will necessarily result in a rearranged

product.

Brown¹⁴⁰ has questioned the validity of a non-classical intermediate during the solvolysis of (137, X=OTS) preferring the possibility of an equilibrating pair of classical tricyclic carbonium ions (141). By carrying out the solvolysis in the presence of hydride it is possible to trap the carbonium ions formed as the hydrocarbon¹⁴³. Using this process Brown isolated the hydrocarbon (139, Y=H) and suggests that this supports a classical ion as intermediate. On the other hand, Brown concedes that in the case of reduction in ether (a slower process) it is unlikely that the ionisation of the tosylate or halide will proceed to any great extent before reduction occurs and discrete carbonium ions are unlikely to be formed.

Another process in hydride reactions with 7-substituted norbornadienes has been observed¹⁴⁴. This is described as a 'solvent - sensitive anionic rearrangement of the carbon skeleton.' Treatment of (137, X=OCOCH₃, OH, OCOPh) with lithium aluminium

hydride in tetrahydrofuran affords high yields of cycloheptatriene. By analogy with the reaction in diethyl ether which results in stereospecific carbon-carbon double bond reduction¹⁴⁵ this process is thought to be intramolecular. The difference between the two reactions is ascribed to the coordinating ability of the solvent and the course of reduction is a function of the Lewis base properties of the solvent or other constituents in the reduction medium. The two different paths are indicated in fig. 2 . In the case of tetrahydrofuran as solvent the intermediate is the anion (142) formed by the complexing of a base in the medium to the aluminium atom. This ion then breaks down as shown to cycloheptatriene.

Skeletal Rearrangement During Reduction of
Bicyclo (2,2,2) oct-5-en-2-ol tosylates

During work on the acid catalysed rearrangement of bicyclic octyl hydrocarbons an attempt was made to prepare bicyclo-[2,2,2]octene (145) from syn-bicyclo [2,2,2] octenyl tosylate (143, X=OTs)¹⁴⁶ m.p. 65-66°, with lithium aluminium hydride in refluxing diethyl ether. Unexpectedly the nuclear magnetic resonance (n.m.r.) of the product indicated that it was predominantly bicyclo [3,2,1]oct-2-ene (146).

The oily anti-toluene-p-sulphonate (144, X=OTs) under identical conditions also gave a major product with a modified skeleton, namely, tricyclo [3,2,1,0^{2,7}] octane (147).

A mixture of syn- and anti- bicyclo [2,2,2] oct-5-en-2-ol was obtained from hydride reduction of bicyclo [2,2,2] octenone¹⁴⁶. Separation of this mixture by preparative thin layer chromatography (t.l.c.) yielded syn-bicyclo [2,2,2] oct-5-en-2-ol (143, X=OH) (70%) m.p. 167-168° and anti-bicyclo [2,2,2] oct-5-en-2-ol (144, X=OH)^{147, 106} (30%) m.p. 168-169°.

These isomers were readily distinguished as the syn alcohol exhibits intra-molecular hydrogen bonding of the hydroxyl to the π -electrons of the double bond. Also the carbinol proton (C-2) in the anti-isomer is at a higher field (5 cycles) than that of the syn isomer be due to shielding by the double bond.¹⁰⁶

The alcohols were then converted in the normal manner into the corresponding toluene-p-sulphonates (tosylates), which were treated with lithium aluminium hydride in refluxing diethyl ether.

The overall product distributions (Table 10) in these reduction reactions were determined directly from g.l.c. peak areas using a carbowax support coated open tubular column at room temperature with a low carrier gas (nitrogen) flow rate. All the products were individually stable to the reaction conditions.

Table 10.

Product distribution (%)¹⁴⁸

	(145)	(146)	(148)	(147)
syn-Tosylate (143, X=OTs)	9	85	0	6
anti-Tosylate (144, X=OTs)	5	0	2	93

No alcohol was formed in these reactions indicating that the bond fission is exclusively carbon-oxygen and that there is little steric hindrance to reduction.

Such product distributions might be expected if the esters were to ionise and the resultant carbonium ions undergo attack with hydride ion from the reagent. Brown and Bell¹⁴³ have suggested that hydride reagents can serve as a trap for carbonium ions during the solvolysis of alkyl halides (vide supra). This possibility is further supported by an examination of the products from acetolysis of these tosylates (143 and 144, X=OTs). Goering⁷⁵ has

shown that acetolysis of the syn tosylate (143, X=OTs) results in complete rearrangement and gives axial-bicyclo [3,2,1] oct-3-en-2-yl acetate (149). This suggests that ionisation of (143, X=OTs) may involve sigma-bond participation with direct formation of the relatively stable allyl cation (150) or the non-classical ion (151) with substantial allylic character. Goering prefers the representation (151) as this accomodates the stereospecificity of the reaction (only the axial isomer (149) is formed) but concedes that it is possible that the allylic ion (150) might undergo exclusive exo attack to give (149). As nucleophilic participation by the solvent is not important, and so the reaction involves discrete carbonium ion intermediates, any concerted processes such as (152, arrows) seems unlikely. The most obvious evidence for double bond participation is the increased rate of acetolysis of (143, X=OTs) relative to the saturated tosylate.

Rate enhancement is also found in the solvolysis of the anti-tosylate (144, X=OTs) and the tricyclic product from this reaction (153) confirms the participation of the double bond.

The reaction product distributions from various solvolyses of these tosylates are shown in table 11.

Table 11.

	(153)	(144, X=OAc)	(154)	(149)
<u>syn</u> -Tosylate (143, X=OTs)				
EtNOAc	-	22	-	78
Acetone ¹⁰⁶				
HOAc/NaAc ⁷⁵	-	-	-	100
<u>anti</u> -Tosylate				
HOAc/NaOAc ¹⁰⁶	20	7	3	-
H ₂ O-ti ₂ CO ₃ ¹⁰⁶	75	16	4	5

It would appear, by comparison of tables 10 and 11, that the products from lithium aluminium hydride reductions of the tosylates are analagous to those obtained by acetolysis, the hydride and acetate ions playing parallel roles. The mechanism of these reactions was examined by reduction of the deuterio-ester (155), which was prepared via lithium aluminium deuteride reduction of bicyclo [2,2,2] octenone, with lithium aluminium hydride in refluxing diethyl ether. The furnished product [1-²H] bicyclo [3,2,1]oct-2-ene, (156) eliminates the possibility of a reaction mechanism involving attack by hydride ion at the methine group adjacent to the ester function (157, arrows) which would lead to [5-²H] bicyclo [3,2,1] oct-2-ene (158).

To establish the structure of (156) the trideuterio olefin (159) was prepared. [2,2',4,4'-²H₄] Bicyclo [3,2,1] octan-3-one, obtained by equilibration in alkaline D₂O of bicyclo [3,2,1] octan-3-one, was reduced to a mixture of the epimeric alcohols (160, X=OH).

The n.m.r spectrum of this mixture showed two singlets at 6.01 and 6.16 corresponding to the carbinol protons of the two alcohols. The absence of all but long range spin-spin coupling with these protons indicated that deuterium insertion had been effective. Conversion into the tosylates (160, X=OTs) and the heating of these esters in refluxing collidine furnished the trideuterio olefin (159). This olefin showed a singlet at τ 4.63 due to the single olefinic proton at C-3 and so allowed assignment of the protons at C-2 (τ 4.12) and C-3 in the complex spectrum of the parent olefin. The diffuse triplet at τ 4.12 in bicyclo (3,2,1) oct-2-ene is collapsed to a diffuse doublet in the monodeuterio-olefin derived from reduction of (155), indicating that the deuterium is at least substantially in the bridgehead position adjacent to the double bond as in (156).

These results exclude any mechanism such as (157, arrows) as the deuterium in position C-5 in the olefin (158) would not greatly alter the n.m.r. pattern of the C-2 (or C-3) olefinic proton.

It is also obvious from these results that there is little, if any, double bond isomerisation during reductive removal of the tosylate group, as this would lead to a scattering of deuterium over the two bridgehead positions, viz. C-1 and C-5. This points to the absence of a discrete cationic intermediate such as (150) in the reduction of these tosylates by lithium aluminium hydride in diethyl ether, and makes it appear likely that hydride capture is a rapid and facile process which occurs synchronously with ionisation of the ester function.

Experimental.

Reduction of Bicyclo (2,2,2) oct-5-en-2-one.-

Bicyclo (2,2,2) oct-5-en-2-one (498 mg.) was treated with lithium aluminium hydride (50 mg.) in diethyl ether at room temperature for 30 minutes. Saturated sodium sulphate (0.1 ml.) was added, followed by anhydrous sodium sulphate. Filtration and removal of solvent afforded a mixture (476 mg.) of the epimeric alcohols (143 and 144, X=OH) which were then separated by preparative thin layer chromatography, (t.l.c.) (solvent, 15% ethyl acetate in light petroleum).

The less polar component was :-

syn-Bicyclo (2,2,2) oct-5-en-2-ol (143, X=OH)

m.p. 167-168° (lit.⁷⁵ 167-169°: n.m.r., b.d. at

τ 6.10 (1H-2; $J = 8$ c./sec.); sextet at τ 3.70

(2H-5,6): i.r., $\nu_{\text{max.}}$ 3615, 3588, 3045, 1120, 1070, 1056, 1030 cm^{-1} .

The more polar component was:-

anti-Bicyclo (2,2,2) oct-5-en-2-ol. (144, X=OH)

m.p. 168-169° (lit.¹⁰⁶ 170-171°): n.m.r., b.d. at τ 6.15 (1H-2; J = 8 c./sec.); m at τ 3.76 (2H-5,6): i.r., V_{\max} . 3618, 3044, 1045 cm^{-1} .

syn-Bicyclo (2,2,2) oct-5-en-2-yl tosylate. (143, X=OTs).-

Chilled solutions of syn-Bicyclo (2,2,2)oct-5-en-2-ol (120 mg.) in dry pyridine (1 ml.) and toluene-p-sulphonyl chloride (290 mg.) in the same solvent (1 ml.) were mixed and allowed to stand at room temperature overnight. The reaction was poured onto ice, extracted with ether and the solvent removed from these extracts in vacuo at room temperature. Crystallisation of the crude product from pentane yielded syn-bicyclo (2,2,2) oct-5-en-2-yl tosylate (143, X=OTs) (210 mg.) m.p. 65-66° (lit.¹⁴⁶ 64-64.5°): n.m.r. b.d. at τ 5.23 (1H-2; J = 8 c./sec.); sextet at τ 3.78 (2H-5,6); s at τ 7.56 (3H-aromatic methyl);, q at τ 2.41 (4H-aromatic H's).

anti-Bicyclo (2,2,2) oct-5-en-2-yl tosylate (144, X=OTs).-

anti-Bicyclo (2,2,2) oct-5-en-2-ol was converted, by the above procedure into the corresponding oily anti-bicyclo (2,2,2) oct-5-en-2-yl tosylate. Both tosylates were unstable but could be stored for some time in a chilled ethereal solution.

Lithium aluminium hydride reduction of the syn- tosylate.-

syn-Bicyclo (2,2,2) oct-5-en-2-yl tosylate (143, X=OTs) (150 mg.) was treated with lithium aluminium hydride (20 mg.) in refluxing diethyl ether for 12 hours. The reaction was worked up as described above and the ether removed at 0°C to give a mixture of hydrocarbons (43 mg.) which was shown by n.m.r. to be predominately bicyclo (3,2,1) oct-2-ene.

The anti-tosylate (144, X=OTs) was reacted in an identical manner and the hydrocarbon products of both reactions were analysed by g.l.c.

[2-²H1] syn-bicyclo (2,2,2) oct-5-en-2-ol.-

Bicyclo (2,2,2) oct-5-en-2-one (240 mg.) was

reduced with lithium aluminium deuteride (38 mg.) in diethyl ether. The usual workup furnished a mixture (235 mg.) from which [2-²H1] syn-bicyclo (2,2,2)oct-5-en-2-ol was isolated by preparative t.l.c. Reaction of this deuterio-alcohol (88 mg.) in dry pyridine (1 ml.) with tosyl chloride (195 mg.) in the same solvent (2 ml.) yielded [2-²H1] syn-bicyclo (2,2,2)oct-5-en-2-yl tosylate (185 mg.): n.m.r., g at τ 2.41 (4H-aromatic H's); sextet at τ 3.79 (2H-5,6); s at τ 7.56 (3H-aromatic methyl).

Lithium aluminium hydride reduction of the deuterio syn-tosylate.-

The deuterio-tosylate (155) (125 mg.) was reacted with lithium aluminium hydride (20 mg.) in refluxing diethyl ether for 12 hours. The crude product was eluted through a short silica column in pentane and the pentane removed at 0°C giving [1-²H1] bicyclo (3,2,1) oct-2-ene (156): n.m.r., b.d. at τ 4.12 (1H-2); m at τ 4.63 (1H-3).

[2,2', 4,4' - $^2\text{H}_4$] Bicyclo (3,2,1) octan-3-one.-

In the manner of Schaeffer and Lark¹⁴⁹ bicyclo (3,2,1) octan-3-one (200 mg.) was dissolved in dioxane (5 ml.) then transferred to an ampoule, D_2O (1 ml.) and sodium (50 mg.) were added and allowed to react before the ampoule was sealed and maintained at 100°C for 7 days. The reaction was cooled, poured into pentane and the organic layer separated. Removal of the solvent furnished the tetradeuterio-ketone (187 mg.).

[2,4,4' - $^2\text{H}_3$] Bicyclo (3,2,1) oct-2-ene.-

The tetradeuterio-ketone (187 mg.) was reduced with lithium aluminium hydride in the usual manner to give a mixture of the isomer tetradeuterio-3-ols (172 mg.): n.m.r., δ at τ 6.01 and τ 6.16, carbinol protons of the isomers).

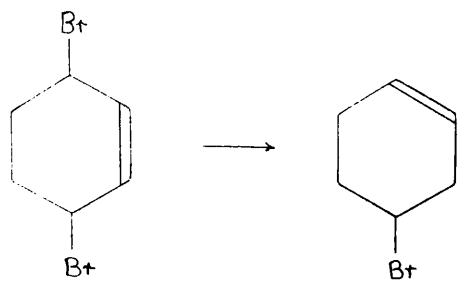
The mixture of alcohols was converted into the corresponding tosylates in the usual manner and the crude tosylate product (350 mg.) treated with refluxing pyridine for 2 hr. The reaction was cooled, poured

into water and the product extracted into pentane.

The pentane washing were combined, washed with dilute hydrochloric acid and saturated aqueous bicarbonate and the solvent dried and removed under vacuum at -5°C .

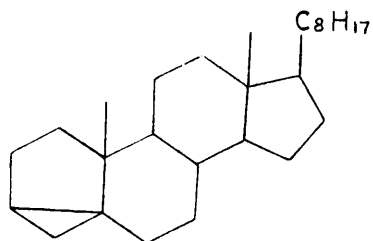
The crude product was eluted through alumina in pentane and sublimed ($0^{\circ}\text{C}/760\text{ mm.}$) to afford $[2,4,4'\text{-}^2\text{H}_3]$

bicyclo (3,2,1) oct-2-ene (72 mg.): n.m.r., $\underline{\text{S}}$ at τ 4.63 (1H-3).

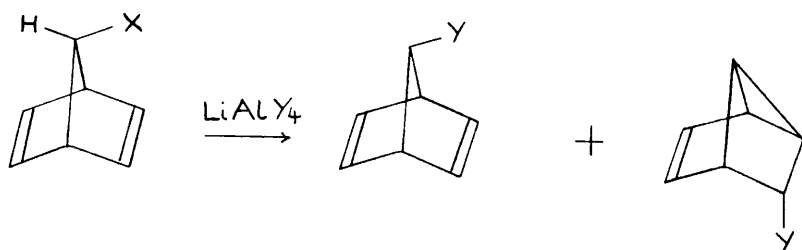


134

135



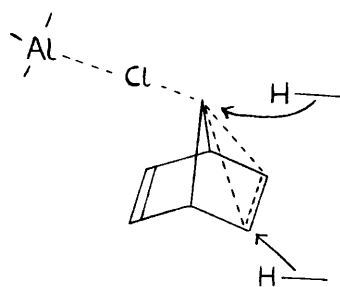
136



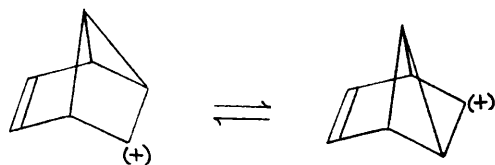
137

138

139

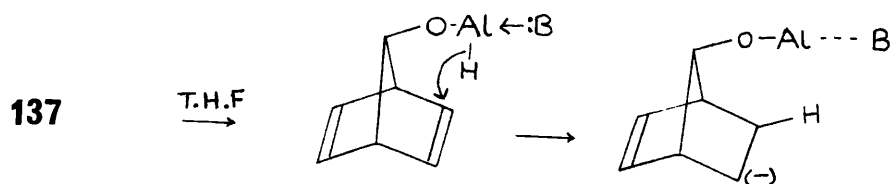
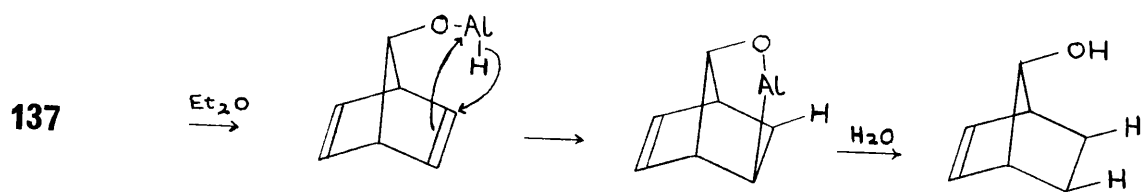


140

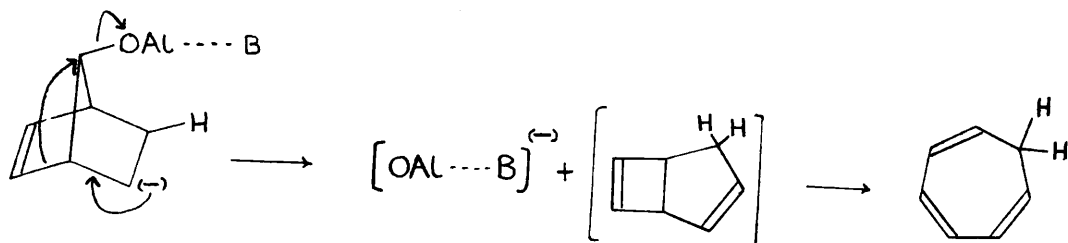


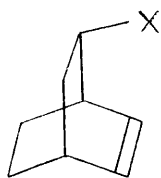
141

Figure 2.



142

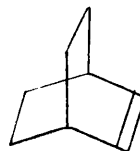




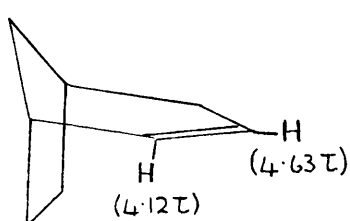
143



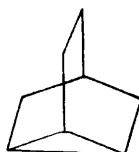
144



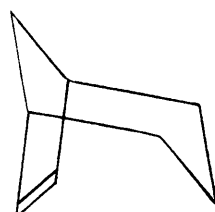
145



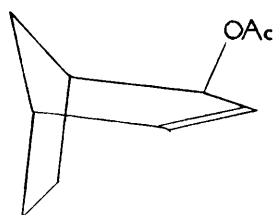
146



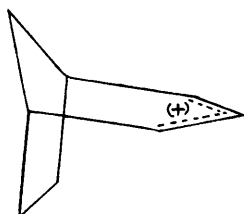
147



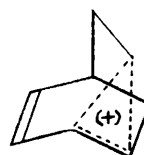
148



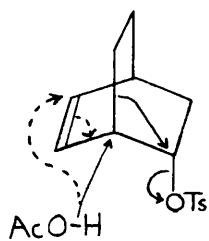
149



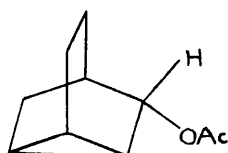
150



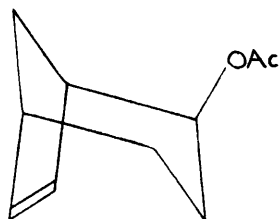
151



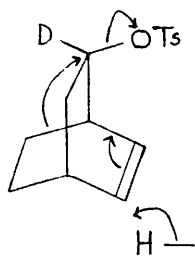
152



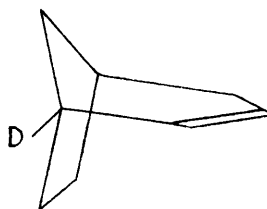
153



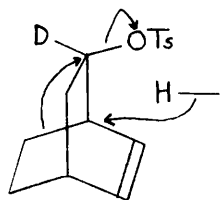
154



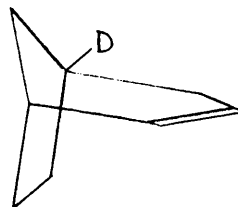
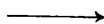
155



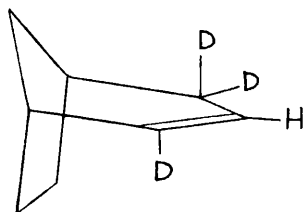
156



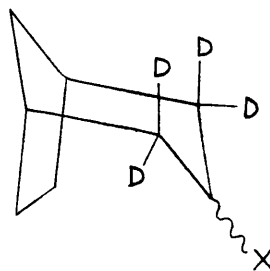
157



158



159



160

References.

1. For leading references see A. Streitwieser, 'Solvolytic Displacement Reactions', p.135, McGraw-Hill Book Co. Inc., 1962.
2. F. N. McElrath, M. Fritz, C. Brown, C. Y. LeGall, and R. B. Duke, J. Org. Chem., 1960, 25, 2195.
3. S. Winstein, B. K. Morse, E. Grunwald, K. C. Shreiber, and J. Corse, J. Amer. Chem. Soc., 1952, 74, 1113.
4. G. LeNy, Thesis, University of Paris, France, 1964.
5. R. S. Bly and H. S. Dryden, Chem. Ind., 1959, 1287.
6. W. G. Dauben and J. B. Rogan, J. Amer. Chem. Soc., 1957, 79, 5002.
7. W. G. Dauben, Bull. Soc. Chim. France, 1964, 11b, 3.
8. P. S. Skell, I. Starer, and A. P. Krapcho, J. Amer. Chem. Soc., *ibid.*, 1960, 82, 5257.

9. G. J. Karabatsos and J. D. Graham, *ibid.*,
1960, 82, 5250.
G. J. Karabatsos, C. E. Orzech, Jr., *ibid.*,
1964, 86, 1994.
10. S. Winstein and H. Marshall, *ibid.*, 1952,
74, 1120.
11. C. C. Lee and M. K. Frost, *Can. J. Chem.*,
1965, 43, 526.
12. W. H. Saunders and R. H. Paine, *J. Amer. Chem.*
Soc., 1961, 83, 882.
13. W. A. Sanderson and H. S. Mosher, *ibid.*,
1961, 83, 5033.
W. A. Sanderson and H. S. Mosher, *ibid.*,
1966, 88, 4185.
14. G. Solladie, M. Muskatirovic and H. S. Mosher,
Chem. Comm., 1968, 809.

15. Reference 1, p.122.
16. J. E. Nordlander, S. P. Jindal, P. Von R. Schleyer, R. C. Fort, J. J. Harper, and R. D. Nicholas, J. Amer. Chem. Soc., 1966, 88, 4475.
17. R. C. Fort and P. Von R. Schleyer, Chem. Rev., 1964, 64, 277.
18. K. B. Wiberg and B. R. Lowry, J. Amer. Chem. Soc., 1963, 85, 3188.
19. R. L. Bixler and C. Niemann, J. Org. Chem., 1958, 23, 742.
20. C. A. Grob, M. Ohta and A. Weiss, Helv. Chim. Acta, 1958, 41, 1191.
21. C. A. Grob, R. M. Hoegerle, and M. Ohta, *ibid.*, 1962, 45, 1823.
22. S. H. Graham and D. A. Jonas, private communication.

23. F. S. Fawcett, 'Bredt's Rule', Chem. Revs., 1950, 47, 219.
24. J. A. Marshall and H. Faubl, J. Amer. Chem. Soc., 1967, 89, 5965.
J. R. Wiseman, *ibid.*, 1967, 89, 5966.
25. J. P. Ferris and N. C. Miller, *ibid.*, 1966, 88, 3522.
26. R. McCrindle and R. Murray, Chem. and Ind., 1964, 500.
27. R. McCrindle, A. Martin and R. Murray, *In press*.
28. P. Lasylo and P. von R. Schleyer, J. Amer. Chem. Soc., 1963, 85, 2017.
29. A. R. H. Cole, G. T. A. Muller, D. W. Thornton and R. L. S. Willix, J. Chem. Soc., 1959, 1218.
30. G. Zweifel and H. C. Brown, Organic Reactions, John Wiley and Sons, Inc., Vol. 13., p.1.
31. L. P. Kuhn, J. Amer. Chem. Soc., 1954, 76, 4323.
32. K. Bowden, I. M. Heilbron, E. R. H. Jones and B. C. L. Weedon, J. Chem. Soc., 1946, 39.
33. S. Sternhell, Rev. Pure Appl. Chem. (Australia), 1964, 14, 15.

34. L. M. Jackman, 'Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry', Pergamon Press, London, 1959, p.85.
35. M. Eakin, Ph.D. Thesis, Glasgow, 1967.
36. N. Rabjohn, Organic Reactions, John Wiley and Sons Inc., New York, Vol. 5, p.331.
37. C. G. Swain and C. R. Morgan, J. Org. Chem., 1964, 29, 2097.
38. A. Streitwieser, 'Solvolytic Displacement Reactions', McGraw-Hill Book Co. Ltd., New York, 1962, p.153.
39. A Streitwieser, 'Molecular Orbital Theory for Organic Chemists', John Wiley and Sons Inc., New York, 1962, p.386.
40. E. Wenkert, Chem. and Ind., 1955, 282.
41. See references 54 and 55.
42. R. A. Appleton, A. J. McAlees, A. McCormick, R. McCrindle, and R. D. H. Murray, J. Chem. Soc., 1966, 2321.
43. G. H. Whitham, 'Alicyclic Chemistry', Oldbourne Press, London, 1963, p.7.

44. J. P. Connelly and R. McCrindle Chem. and Ind.,
1965, 379.
45. D. H. Williams and N. S. Bhacca, Tetrahedron,
1965, 21, 2021.
46. R. R. Sobti and S. Dev., Tetrahedron Letters,
1966, 3939.
47. Y. Kitahara and A. Yoshikoshi, *ibid.*, 1964, 1771.
48. M. Kitadani, H. Uda, A. Yoshikoshi, *ibid.*, 1966,
4843.
49. G. Hugel, L. Lods, J. M. Mellor and G. Ourisson,
Bull. Soc. Chim., France, 1965, 2894.

50. S. Winstein and D. S. Trifan, J. Amer. Chem. Soc., 1949, 71, 2953.
51. S. Winstein and D. S. Trifan, *ibid.*, 1952, 1147, 1154.
52. T. P. Nevell, E. de Salas and C. L. Wilson, J. Chem. Soc., 1939, 1188.
53. For leading references see:-
H. C. Brown and M. H. Rei, J. Amer. Chem. Soc., 1964, 86, 5008. and S. Winstein, *ibid.*, 1965, 87, 381.
54. J. D. Roberts and C. C. Lee, *ibid.*, 1951, 73, 5009.
55. J. D. Roberts, C. C. Lee and W. H. Saunders, *ibid.*, 1954, 76, 4501.
56. M. F. Ansell and M. S. Dewar, Nature, 1954, 173, 898.
57. P. Von R. Schleyer, G. A. Olah, W. E. Watts, R. C. Fort and M. B. Comisarow, J. Amer. Chem. Soc., 1964, 86, 5679.
58. M. Saunders, P. Von R. Schleyer and G. A. Olah, *ibid.*, 1964, 86, 5680.
59. W. Von E. Doering and A. P. Wolf, XIIth International Congress of Pure and Applied Chemistry, New York, 1950, p.437.

60. G. Komppa and G. A. Nyman, *Ann.*, 1938, 535, 252.
61. C. E. Dills, Thesis, Harvard University, 1955.
62. C. C. Lee and L. K. M. Lam, *J. Amer. Chem. Soc.*, 1966, 88, 2831.
63. A. Colter, E. C. Friedrich, N. J. Holmes and S. Winstein, *ibid.*, 1965, 87, 37.
64. J. A. Berson and P. W. Grubb, *ibid.*, 1965, 87, 4016.
65. B. M. Benjamin and C. J. Collins, *ibid.*, 1966, 88, 1556.
66. C. J. Collins, Z. K. Cheema, R. G. Werth and B. M. Benjamin, *ibid.*, 1964, 86, 4913.
67. B. M. Benjamin, B. W. Ponder and C. J. Collins, *ibid.*, 1966, 88, 1558.
68. R. A. Appleton and S. H. Graham, *Chem. Comm.*, 1965, 297.
69. R. A. Appleton, J. R. Dixon, J. M. Evans and S. H. Graham, *Tetrahedron*, 1967, 23, 805.
70. W. A. C. Brown, J. Martin and G. A. Sim, *J. Chem. Soc.*, 1965, 1844.

71. K. B. Wiberg and B. A. Hess, J. Org. Chem., 1966, 31, 2250.
72. H. M. Walborsky, J. Webb and C. G. Pitt, J. Org. Chem., 1963, 28, 3214.
73. H. M. Walborsky, M. E. Baum and A. A. Youssef, J. Amer. Chem. Soc., 1961, 83, 988.
74. R. R. Sauers and J. A. Biesler, Tetrahedron Letters, 1964, 2181.
75. H. L. Goering and M. F. Sloan, J. Amer. Chem. Soc., 1961, 83, 1397, 1992.
76. S. Winstein and P. Carter, J. Amer. Chem. Soc., 1961, 83, 4485.
77. G. Dann Sargent, Quart. Rev., 1966, 20, 301, and references cited therein.
78. 'Molecular Orbital Theory for Organic Chemists' by A. Streitwieser, John Wiley and Sons Inc., New York, 1962, p.386.
79. R. Hoffmann, J. Chem. Phys., 1964, 40, 2480.
80. J. A. Berson and D. Willner, J. Amer. Chem. Soc., 1964, 86, 609.
81. K. B. Wiberg and B. A. Hess, J. Amer. Chem. Soc., 1966, 88, 4433.

82. Professor Wiberg mentions in this paper that his results are very similar to those found by Professor H. L. Goering and Dr. T. Padmanathan for the solvolysis of (93 and 94, R=OBs), unpublished results.
83. Goering and Sloan⁵ have reported treating (97) under these conditions, but make no mention of detecting (93, R=OAc).
84. G. LeNy, Compt. Rend., 1960, 251, 1526.
85. J. A. Berson and M. S. Poonian, J. Amer. Chem. Soc., 1966, 88, 170.
86. H. L. Goering and G. N. Fickes, *ibid.*, 1968, 90, 2856.
87. H. Krieger, Suomen Kemistilehti, 1965[B] 38 (11), 160.
88. J. V. Braun and J. Reity, Ber., 1941, 74, 273; K. Alder, H. Krieger and H. Weiss, *ibid.*, 1955, 88, 144; R. C. de Selms and C. M. Combs, J. Org. Chem., 1963, 28, 2206.
89. N. A. Le Bel, J. E. Huber and L. H. Zalkow, J. Amer. Chem. Soc., 1962, 84, 2226; A. F. Bickel, J. Knotnerus, E. C. Kooyman and G. C. Vegter, Tetrahedron, 1960, 2, 230;

- H. M. Walborsky and D. Loncrini, J. Amer. Chem. Soc., 1954, 76, 5396;
- K. Tori, Y. Takano and K. Kitahonoki, Ber., 1964, 27, 2798.
90. C. A. Grob and J. Hostynek, Helv. Chim. Acta, 1963, 46, 1676.
91. A. A. Youssef, M. E. Baum and H. M. Walborsky, J. Amer. Chem. Soc., 1959, 81, 4709.
92. G. Stork, A. Brissolava, H. Landesman, J. Symuszkowicz, and R. Terrell, *ibid.*, 1963, 85, 207.
93. W. Kraus, Ber., 1964, 27, 2719.
94. B. Waegell and C. W. Jefford, Bull. Soc. Chim. France, 1964, 844.
95. W. von Doering, E. T. Fossel and R. L. Kaye, Tetrahedron, 1965, 21, 25.
96. H. C. Brown and F. J. Chlonpek, J. Amer. Chem. Soc., 1963, 85, 2322.
97. H. C. Brown and H. M. Bell, *ibid.*, 1963, 85, 2324.
98. G. Dann Sargent, Quart. Rev., 1966, 20, 301 and references cited therein.
99. P. von R. Schleyer, J. Amer. Chem. Soc., 1964, 86, 1854, 1856.

100. C. S. Foote, J. Amer. Chem. Soc., 1964, 86, 1853.
101. M. J. S. Dewar, Ann. Reports, 1951, 48, 118.
102. S. Winstein and R. Adams, J. Amer. Chem. Soc., 1948, 70, 838.
103. S. Winstein, M. Shatovsky, C. Norton and R. B. Woodward, *ibid.*, 1955, 77, 4183.
104. S. Winstein and M. Shatavsky, *ibid.*, 1956, 78, 592.
105. M. Simonetta and S. Winstein, *ibid.*, 1954, 76, 18.
106. N. A. LeBel and J. E. Huber, *ibid.*, 1963, 85, 3193.
107. R. G. Lawton, *ibid.*, 1961, 83, 2399.
108. P. D. Barlett and S. Bank, *ibid.*, 1961, 83, 2591.
109. M. J. S. Dewar, J. Chem. Soc., 1946, 406.
110. See reference 78.
111. M. Hanack and W. Kaiser, Ang. Chem., 1964, 76, 572.
112. A. C. Cope, D. L. Nealy, P. Scheiner and G. Wood, J. Amer. Chem. Soc., 1965, 87, 3130.
113. H. Felkin, G. LeNy, C. Lion, W. D. K. Macrosson, J. Martin and W. Parker, Tetrahedron Letters, 1966, 157.

114. K. H. Baggle, J. R. Dixon, J. M. Evans and S. H. Graham, *Tetrahedron*, 1967, 23, 299.
115. P. D. Barlett, E. M. Nicholson and R. Owyang, *Tetrahedron*, Suppl. 8, Part 2, 1966, 399.
116. P. D. Barlett, W. S. Trahanovsky, D. A. Bolon and G. H. Schmid, *J. Amer. Chem. Soc.*, 1965, 87, 1314.
117. W. S. Trahanovsky, M. P. Doyle and P. D. Barlett, *J. Org. Chem.*, 1967, 32, 150.
118. E. L. Alfred, J. Sonnenberg and S. Winstein, *J. Org. Chem.*, 1960, 25, 26.
119. W. E. Bachmann and W. S. Strure, *Organic Reaction*, John Wiley and Sons Inc., New York, 1942, Vol. 1, p.38.
120. L. W. Trevoy and W. G. Brown, *J. Amer. Chem. Soc.*, 1949, 71, 1675.
121. E. L. Eliel, *ibid.*, 1949, 71, 3970.
122. E. R. Alexander, *ibid.*, 1950, 72, 3796.
123. H. Schmid and P. Karrer, *Helv. Chim. Acta*, 1949, 32, 1371.
124. H. Gilman and J. J. Beaber, *J. Amer. Chem. Soc.*, 1923, 45, 839., 1925, 47, 578.
125. P. Karrer and G. Widmark, *Helv. Chim. Acta.*, 1951, 34, 34.

126. H. Rapoport and R. M. Bonner, J. Amer. Chem. Soc., 1951, 73, 2872.
127. P. Karrer and P. Dunkel, Helv. Chim. Acta., 1953, 36, 122.
128. P. Karrer and K. Ehrhardt, *ibid.*, 1951, 34, 2202.
129. G. W. Kenner and M. A. Murray, J. Chem. Soc., 1950, 406.
130. J. H. Chapman, J. Elks, G. H. Phillips and L. J. Wyman, *ibid.*, 1956, 4344.
131. D. H. R. Barton and C. J. W. Brooks, *ibid.*, 1951, 257.
132. J. Strating and H. J. Backer, Rec. Trav. Chim., 1950, 69, 638.
133. P. Karrer, H. Asmis, K. N. Sareen and R. Schuzzer, Helv. Chim. Acta., 1952, 35, 427.
134. P. Karrer, H. Asmis, K. N. Sareen and R. Schuzzer, *ibid.*, 1951, 34, 1022.
135. D. J. Cram, J. Amer. Chem. Soc., 1952, 74, 2149.
136. D. H. Cram, F. A. A. Elhafey and H. Weingartner, *ibid.*, 1953, 75, 2293.
137. L. F. Hatch and G. Bachmann, Ber., 1964, 97, 132.

- 138. L. F. Hatch and R. E. Gilbert, J. Org. Chem., 1959, 24, 1811.
- 139. P. R. Story, J. Amer. Chem. Soc., 1961, 83, 3347.
- 140. H. C. Brown and H. M. Bell, *ibid.*, 1963, 85, 2324.
- 141. S. Winstein, A. H. Lewin and K. C. Pande, *ibid.*, 1963, 85, 2324.
- 142. S. Winstein and C. Ordronneau, *ibid.*, 1962, 82, 2084.
- 143. H. C. Brown and H. M. Bell, J. Org. Chem., 1962, 27, 1928.
- 144. B. Franzus and E. I. Snyder, J. Amer. Chem. Soc., 1963, 85, 3902.
- 145. P. R. Story, J. Org. Chem., 1961, 26, 287.
- 146. H. L. Goering, R. W. Greiner and M. F. Sloan, J. Amer. Chem. Soc., 1961, 83, 1391.
- 147. R. R. Fraser and S. O'Farrell, Tetrahedron Letters, 1-62, 1143.
- 148. See Chapter 3 for the preparation of the reference hydrocarbons.
- 149. S. P. Schaeffer and J. C. Lark, J. Org. Chem., 1965, 30, 1337.